

FILE 'HOME' ENTERED AT 18:04:40 ON 19
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=> file medline caplus cancerlit embase
biosis
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FULL ESTIMATED COST
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FILE 'MEDLINE' ENTERED AT 18:05:05 ON
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ABSTRACTS INC.(R)

=> s sepsis or septicemia or septic (W)
disorder

L1 154301 SEPSIS OR SEPTICEMIA
OR SEPTIC (W) DISORDER

=> s interleukin-6 or 1l-6

L2 119260 INTERLEUKIN-6 OR 1L-6

=> s l1 (s) l2

L3 1955 L1 (S) L2

=> s serum (w) levels

L4 122388 SERUM (W) LEVELS

=> s l3 (s) l4

L5 137 L3 (S) L4

=> duplicate remove l5

DUPLICATE PREFERENCE IS 'MEDLINE,
CAPLUS, CANCERLIT, EMBASE, BIOSIS'
KEEP DUPLICATES FROM MORE THAN
ONE FILE? Y/(N):n
PROCESSING COMPLETED FOR L5
L6 43 DUPLICATE REMOVE L5 (94
DUPLICATES REMOVED)

=> d l6 1- ibib,abs

YOU HAVE REQUESTED DATA FROM 43
ANSWERS - CONTINUE? Y/(N):y

L6 ANSWER 1 OF 43 MEDLINE
DUPLICATE 1
ACCESSION NUMBER: 2003003128
MEDLINE
DOCUMENT NUMBER: 22386813
PubMed ID: 12500222
TITLE: Elevated serum levels of the
type I and type II receptors
for tumor necrosis factor-alpha
as predictive factors for
ARF in patients with septic
shock.

AUTHOR: Iglesias Jose; Marik Paul
E; Levine Jerrold S

CORPORATE SOURCE: Department of
Internal Medicine; Robert Wood Johnson
School

of Medicine, Neptune, NJ, USA.
(Norasept II Study
Investigators).

miglesias@erols.com

CONTRACT NUMBER: DK59793 (NIDDK)
HL69722 (NHLBI)

SOURCE: AMERICAN JOURNAL
OF KIDNEY DISEASES, (2003 Jan) 41 (1)
62-75.

Journal code: 8110075. ISSN:
1523-6838.

PUB. COUNTRY: United States

DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL

ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200301

ENTRY DATE: Entered STN:
20030103

Last Updated on STN:
20030118

Entered Medline: 20030117
AB BACKGROUND: Acute renal failure
(ARF), a common and serious complication
in patients with septic shock, has high
mortality. Recent data suggest

that proinflammatory cytokines may contribute to sepsis -associated ARF. METHODS: To examine the role of proinflammatory cytokines, we evaluated 537 patients enrolled in the placebo arm of the Norasept II study, of whom 112 patients (20%) developed ARF. RESULTS: By univariate analysis, the following factors were significantly associated with the development of ARF: male sex, younger age, increased heart rate, higher Acute Physiology and Chronic Health Evaluation II score, oliguria, increased blood urea nitrogen level, increased serum creatinine (Scr) level, decreased arterial pH, and increased serum potassium level.

Although there were no statistically significant differences in serum levels of tumor necrosis factor-alpha (TNF-alpha) or interleukin-6 between patients with and without

ARF, elevated serum levels of the two soluble TNF-alpha receptors (S-TNF-RI and S-TNF-RII) were strongly associated with the development of ARF (S-TNF-RI, 25 +/- 16 versus 18 +/- 13 ng/mL; P = 0.00006; S-TNF-RII, 25 +/- 21 versus 18 +/- 17 ng/mL; P = 0.0007). Using forward stepwise regression analysis, elevated S-TNF-R level remained an independent predictor for ARF, even when we limited our analysis to patients with Scr levels of 1.4 mg/dL or less (< or =124 micromol/L) at study entry, suggesting that decreased renal clearance of S-TNF-R alone cannot account for this association. Elevated S-TNF-R level also was an independent predictor of mortality among patients developing ARF.

CONCLUSION: S-TNF-R level is an independent predictor for the development of ARF and mortality. We speculate that elevated S-TNF-R levels may reflect a more intense inflammatory response.

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L6 ANSWER 2 OF 43 BIOSIS
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ACCESSION NUMBER: 2002:387188

BIOSIS

DOCUMENT NUMBER:

PREV200200387188

TITLE: Protective effects of anti-IL-6 antibody treatment in sepsis.

AUTHOR(S): Neff, Thomas A. (1); Riedemann, N. C. (1); Guo, R. F. (1); Laudes, I. (1); Sarma, V. (1); Ward, P. A. (1)

CORPORATE SOURCE: (1) Pathology, University of Michigan, 1301 Catherine St., Ann Arbor, MI, 48109-0602

USA

SOURCE: FASEB Journal, (March 20, 2002) Vol. 16, No. 4, pp. A592.

<http://www.fasebj.org/>. print.
Meeting Info.: Annual Meeting of the Professional Research Scientists on Experimental Biology New Orleans, Louisiana, USA April 20-24, 2002
ISSN: 0892-6638.

DOCUMENT TYPE: Conference

LANGUAGE: English

AB The glycoprotein interleukin-6 plays a key role in the regulation of cell growth and inflammation and in the acute phase reaction

during the inflammatory process. It has been demonstrated that IL-6 serum levels are strongly increased during

sepsis when compared to healthy individuals. In this study we investigated the effects of anti-IL-6 antibody treatment in cecal ligation and puncture (CLP)-induced sepsis in mice. Animals treated with

a monoclonal anti mouse IL-6 antibody administered intravenously directly after CLP showed a dose dependent improved survival, seven days after induction of sepsis when compared to IgG control injected animals. 6 hours after CLP serum levels of IL-6 were

significantly decreased in anti-IL-6 treated animals (40 ug/animal) when compared to animals treated with the IgG control. In addition we found evidence that anti-IL-6 treated animals showed low serum

levels of TNF α , 6 hours after CLP, while IgG injected control animals showed no detectable TNF α levels in the serum. The suppression of bioactive IL-6 serum levels in the onset of sepsis may therefore alter the acute inflammatory response with resulting beneficial effects on survival.

L6 ANSWER 3 OF 43 MEDLINE
DUPLICATE 2
ACCESSION NUMBER: 2002003486
MEDLINE
DOCUMENT NUMBER: 21623714
PubMed ID: 11750194
TITLE: Early diagnostic markers for neonatal sepsis: comparing C-reactive protein, interleukin-6, soluble tumour necrosis factor receptors and soluble adhesion molecules.
AUTHOR: Dollner H; Vatten L; Austgulen R
CORPORATE SOURCE: Department of Paediatrics, University Hospital of Trondheim, N-7006 Trondheim, Norway..
henrik.dollner@medisin.ntnu.no
SOURCE: JOURNAL OF CLINICAL EPIDEMIOLOGY, (2001 Dec) 54 (12) 1251-7.
Journal code: 8801383. ISSN: 0895-4356.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200201
ENTRY DATE: Entered STN: 20020102
Last Updated on STN: 20020131
Entered Medline: 20020130

AB We compared six inflammatory mediators (C-reactive protein (CRP), interleukin-6 (IL-6), soluble tumour necrosis factor receptors (p55 and p75) and soluble adhesion molecules (ICAM-1, E-selectin)) as early diagnostic tests for neonatal sepsis, and studied the possible benefit of combining parameters. Blood samples were

obtained from 166 consecutively admitted neonates, who were suspected to suffer from infection within the first week of life. Neonates were retrospectively classified as infected (sepsis, clinical sepsis or pneumonia), possibly infected, or non-infected.

Twenty-four infected neonates had higher serum levels of all six mediators (all $P < 0.05$), and 18 possibly infected neonates had higher levels of CRP, IL-6, ICAM-1 and E-selectin (all $P < 0.05$), than neonates without infection ($n = 124$). Receiver operator characteristic plots showed that CRP was the single best diagnostic test. Multiple logistic regression modelling, including various combinations of two to six mediators, consistently showed that IL-6, in addition to CRP, predicted sepsis. With infected and possibly infected neonates as the reference standard, a combined test of CRP ≥ 10 mg/l and/or IL-6 ≥ 20 pg/ml had a sensitivity of 85%, specificity of 62%, and negative likelihood ratio of 0.24. Using infected neonates as reference standard alone, and including possibly infected as controls, sensitivity increased to 96%, whereas specificity decreased to 58%; a negative test result (CRP < 10 mg/l and IL-6 < 20 pg/ml) ruled out sepsis with high certainty (likelihood ratio = 0.07). CRP performed best as a diagnostic test for neonatal sepsis. Diagnostic accuracy was further improved by combining CRP and IL-6, whereas the other parameters (p55, p75, ICAM-1 and E-selectin) added no further diagnostic information.

L6 ANSWER 4 OF 43 MEDLINE
DUPLICATE 3
ACCESSION NUMBER: 2002349110
MEDLINE
DOCUMENT NUMBER: 22087500
PubMed ID: 12092128
TITLE: [Chorioamnionitis and early-onset neonatal sepsis do not significantly affect levels of interleukin-6 in very low birth weight neonates].

Chorioamniitis a casna
novorozenecka sepse neovlivnuji
vznamne hladinu interleukinu-
6 u novorozencu velmi nizke
porodni hmotnosti.

AUTHOR: Janota J; Stranak Z;
Belohlavkova S; Jirasek J E
CORPORATE SOURCE: Ustav pro peci o
matku a dite, Podolske nabrezi 157, 147 10
Praha 4-Podoli, Czech

Republic.

SOURCE: SBORNIK LEKARSKY,
(2001) 102 (3) 411-8.

Journal code: 0025770. ISSN:

0036-5327.

PUB. COUNTRY: Czech Republic

DOCUMENT TYPE: Journal; Article;

(JOURNAL ARTICLE)

LANGUAGE: Czech

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200208

ENTRY DATE: Entered STN:

20020703

Last Updated on STN:

20020809

Entered Medline: 20020808

AB OBJECTIVE: To determine the
influence of maternal chorioamnionitis and
neonatal sepsis on interleukin-6 (IL-6)
levels in cord blood and in blood obtained
from very low birth weight

(VLBW) infants within the first two hours
of life. DESIGN: Prospective

clinical study. SETTING: Institute for the
Care of Mother and Child,

Prague. METHODS: We measured the
serum levels of IL-6

in 30 consecutive VLBW infants born in
our institute. IL-6 levels were

evaluated in cord blood and in neonatal
blood within 2 hours after

delivery. Maternal chorioamnionitis and
neonatal sepsis within

the first 72 hours of life were monitored.

RESULTS: Maternal

chorioamnionitis was detected in 7 of 30
patients (23.3%). There was no

significant increase in IL-6 level in cord
blood of newborns with maternal

chorioamnionitis ($p = 0.42$). Serum level
of IL-6 in this group did not

differ from the level in newborns of
mothers without signs of

intraamniotic infection ($p = 0.39$).

Neonatal early-onset sepsis

was diagnosed in 7 of 30 patients
(23.3%). There was no influence of
neonatal sepsis on IL-6 level in cord
blood ($p = 0.98$) and IL-6

level in neonatal blood ($p = 0.19$). We did
not find any correlation

between the group "chorioamnionitis
positive" and "sepsis

positive" ($p = 0.31$). CONCLUSION: IL-6
in cord blood or in neonatal blood

within 2 hours of life was not enough
sensitive and specific marker of

maternal chorioamnionitis as well as for
early-onset neonatal

sepsis in the group of very low birth
weight infants.

L6 ANSWER 5 OF 43 CAPLUS

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ACCESSION NUMBER: 2001:443273

CAPLUS

DOCUMENT NUMBER: 136:181587

TITLE: Detection of cytokine
level in cord blood for early

diagnosis of neonatal sepsis

AUTHOR(S): Jin, Yalei; Wang,
Xueqin; Yu, Liping; Zhang, Yuhou

CORPORATE SOURCE: Department of
Pediatrics, Zhongnan Hospital, Wuhan
University, Wuhan, 430071,

Peop. Rep. China

SOURCE: Wuhan Daxue
Xuebao, Yixueban (2001), 22(1), 87-88

CODEN: WDXYYA

PUBLISHER: Wuhan Daxue
Jikanshe

DOCUMENT TYPE: Journal

LANGUAGE: Chinese

AB The serum levels of interleukin-6

(IL-6) and tumor necrosis factor-.alpha.
(TNF.alpha.) in neonatal

sepsis as biomarker for early diagnosis of
neonatal sepsis

were studied. Serum levels of IL-6 and
TNF.alpha. in cord blood of 20

cases with sepsis and 52 healthy controls
were detd. by ELISA. The serum

level of IL-6 was significantly higher in
neonatal sepsis group (0.026

6-1.258 9 ng mL⁻¹) than in control (0.021
1-0.053 1 ng mL⁻¹). The serum

level of TNF.alpha. was also significantly
higher in neonatal sepsis group

(0.65-12.60 ng mL⁻¹) than in control.

The results showed that the serum

levels of IL-6 and TNF.alpha. in cord blood can be used as a biomarker of neonatal sepsis, and IL-6 had higher sensitivity and specificity than TNF.alpha..

L6 ANSWER 6 OF 43 MEDLINE
DUPLICATE 5
ACCESSION NUMBER: 2001534619
MEDLINE
DOCUMENT NUMBER: 21465323
PubMed ID: 11581469
TITLE: Reactive hyperemia and interleukin 6, interleukin 8, and tumor necrosis factor-alpha in the diagnosis of early-onset neonatal sepsis.
AUTHOR: Martin H; Olander B; Norman M
CORPORATE SOURCE: Department of Women and Child Health, Division of Neonatology, Karolinska Hospital, Sweden..
helena.martin@kbh.ki.se
SOURCE: PEDIATRICS, (2001 Oct) 108 (4) E61.
Journal code: 0376422. ISSN: 1098-4275.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index
Medicus Journals; Priority Journals
ENTRY MONTH: 200201
ENTRY DATE: Entered STN: 20011003

Last Updated on STN: 20020125
Entered Medline: 20020103
AB OBJECTIVE: To evaluate the diagnostic value of peripheral circulatory reactive hyperemia and serum levels of interleukin-6 (IL-6), IL-8, and tumor necrosis factor-alpha (TNF-alpha) in early-onset neonatal sepsis.
METHODS: Reactive hyperemia in the dorsal hand and serum levels of IL-6, IL-8, and TNF-alpha were studied in newborn infants (n = 32; gestational age 39 +/- 3 weeks) who had been admitted to the neonatal unit because of suspected sepsis <48 hours after

birth. On admission, reactive hyperemia after a standardized arterial occlusion was measured with laser Doppler technique, and blood samples were taken for cytokine analyses. On the basis of predetermined criteria, the infants subsequently were classified as septic (n = 12) or not (n = 20). RESULTS: The degree of reactive hyperemia was higher in the group with sepsis (median + 170% perfusion increase) than in that without (+37%). On admission, serum levels of IL-6, IL-8, and TNF-alpha all were higher in septic (median values: 1620, 331, and 22 pg/mL, respectively) than in nonseptic neonates (median values: 42, 63, and 13 pg/mL, respectively). In the group with sepsis, the degree of reactive hyperemia correlated to log IL-6 (r = 0.80) and log IL-8 values (r = 0.71). CONCLUSION: Newborn infants with septicemia have increased reactive hyperemia and elevated cytokine levels very early in their disease. Reactive hyperemia in skin can be analyzed at the bedside and noninvasively and therefore may serve as an additional diagnostic tool in neonatal sepsis.

L6 ANSWER 7 OF 43 MEDLINE
DUPLICATE 6
ACCESSION NUMBER: 2001383763
MEDLINE
DOCUMENT NUMBER: 21246625
PubMed ID: 11348793
TITLE: Interleukin-6 and C-reactive protein serum levels in sepsis-related fatalities during the early postmortem period.
AUTHOR: Tsokos M; Reichelt U; Jung R; Nierhaus A; Puschel K
CORPORATE SOURCE: Institute of Legal Medicine, University of Hamburg, Butenfeld 34, D-22529, Hamburg, Germany.. mtsokos@ngi.de
SOURCE: FORENSIC SCIENCE INTERNATIONAL, (2001 Jun 1) 119 (1) 47-56.
Journal code: 7902034. ISSN: 0379-0738.

PUB. COUNTRY: Ireland
DOCUMENT TYPE: Journal; Article;
(JOURNAL ARTICLE)

(VALIDATION STUDIES)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200107
ENTRY DATE: Entered STN:
20010709

Last Updated on STN:

20010709

Entered Medline: 20010705

AB Postmortem interleukin-6 (IL-6) and C-reactive protein

(CRP) serum levels were investigated prospectively in

sepsis-related fatalities and non-septic fatalities by using a

linear regression model. At least three blood samples were collected

between 0.3 and 139 h postmortem from sepsis-related fatalities

(n=8) and non-septic fatalities (n=16). In

addition, one antemortem blood

sample was collected shortly before death from the septic patients.

Antemortem and postmortem IL-6 and CRP levels were highly elevated in all

individuals included in the sepsis group.

An excessive

postmortem increase of IL-6 serum levels associated

with progressive time after death was observed in five out of the eight

septic patients. Both, IL-6 and CRP serum concentrations seem to be

suitable biochemical postmortem markers of sepsis. The

determination of IL-6 serum levels above 1500 pg/ml in

peripheral venous blood obtained in the early postmortem interval can be

considered as a diagnostic hint towards an underlying septic condition. A

more precise postmortem discrimination between sepsis and

non-septic underlying causes of death is provided by the postmortem

measurement of serum CRP in

peripheral venous blood: on condition that at least two postmortem CRP values have

been determined at different time

points postmortem, the CRP level of a deceased at the time of death can be

calculated by using linear regression analysis. When assessing postmortem

IL-6 and CRP concentrations as biochemical postmortem markers of sepsis, various clinical conditions, such as a preceding trauma or burn injury going along with elevated IL-6 and/or CRP levels prior to death as a result of the systemic inflammatory response syndrome (SIRS) should be taken into consideration, thus adding relevant information for the practical interpretation of the results.

L6 ANSWER 8 OF 43 MEDLINE
DUPLICATE 7

ACCESSION NUMBER: 2001276023
MEDLINE

DOCUMENT NUMBER: 21259571

PubMed ID: 11359438

TITLE: Suppression of the clinical and cytokine response to

endotoxin by RWJ-67657, a p38 mitogen-activated

protein-kinase inhibitor, in healthy human volunteers.

AUTHOR: Fijen J W; Zijlstra J G; De Boer P; Spanjersberg R; Cohen

Tervaert J W; Van Der Werf T S; Ligtenberg J J; Tulleken J

E

CORPORATE SOURCE: Intensive and Respiratory Care Unit and Division of

Immunology, Department of Internal Medicine, University

Hospital Groningen, Groningen, The Netherlands..

j.w.fijen@int.azg.nl

SOURCE: CLINICAL AND EXPERIMENTAL IMMUNOLOGY, (2001 Apr) 124 (1)

16-20.

Journal code: 0057202. ISSN:

0009-9104.

PUB. COUNTRY: England: United Kingdom

DOCUMENT TYPE: (CLINICAL TRIAL) Journal; Article; (JOURNAL

ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200106

ENTRY DATE: Entered STN:

20010618

Last Updated on STN:

20010618

Entered Medline: 20010614

AB Sepsis resulting in multiorgan failure and death is still a major problem in intensive care medicine, despite extensive attempts to interfere in the supposed underlying mechanism of a deranged immune system. This is not only due to the persistent lacunae in knowledge about the immune system in sepsis but also due to the lack of sufficient instruments for intervention. Inhibitors of the p38 mitogen-activated protein kinase (p38MAPK) have been used to study the signalling pathway of the immune response. In vitro and animal studies have demonstrated that blocking p38MAPK could mitigate the pro-inflammatory response and improve survival after endotoxaemia. Using an endotoxaemia model in healthy human volunteers we evaluated the attenuation of clinical and cytokine response to endotoxin after inhibition of p38MAPK by an oral dose of RWJ-67657, a pyridinyl imidazole. We measured the clinical parameters temperature, blood pressure and heart rate. The proinflammatory cytokines tumour necrosis factor-alpha, interleukin-6 and interleukin-8 were measured by ELISA at various points during a 24-h period. Drug toxicity was evaluated by routine clinical and laboratory examinations. After a single dose of RWJ-67657 the temperature and blood pressure response remained at the basal level. The inhibition of TNF-alpha, IL-6 and IL-8 response was a dose dependent. With the maximum dosage, reduction in peak serum levels of the proinflammatory cytokines was greater than 90%. There was no drug-related toxicity. Interpretation: We conclude that inhibition of p38MAPK by RWJ-67657 might be a tool to intervene in the deranged immune response in sepsis and other inflammatory diseases.

L6 ANSWER 9 OF 43 MEDLINE
 DUPLICATE 8
 ACCESSION NUMBER: 2000255422
 MEDLINE

DOCUMENT NUMBER: 20255422
 PubMed ID: 10792949
 TITLE: The effects of interleukin-10 in hemorrhagic shock.
 AUTHOR: Karakozis S; Hinds M; Cook J W; Kim D; Provido H; Kirkpatrick J R
 CORPORATE SOURCE: Department of Surgery, Washington Hospital Center, 110 Irving Street NW, Washington, DC 20010-2975, USA.
 SOURCE: JOURNAL OF SURGICAL RESEARCH, (2000 May 15) 90 (2) 109-12.
 Journal code: 0376340. ISSN: 0022-4804.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200006
 ENTRY DATE: Entered STN: 20000622
 Last Updated on STN: 20000622
 Entered Medline: 20000614
 AB BACKGROUND: Interleukin-10 (IL-10) counteracts the effects of the proinflammatory cytokines interleukin-1 (IL-1), interleukin-6 (IL-6), and tumor necrosis factor (TNF). Experimental data suggest that inhibition of these proinflammatory cytokines improves outcome in sepsis, endotoxemia, necrotizing pancreatitis, and other severe inflammatory states. We hypothesized that the administration of IL-10 would attenuate the release of proinflammatory cytokines after severe hemorrhagic shock. METHODS: To test our hypothesis, male Sprague-Dawley rats (N = 20) were divided into control and experimental groups. We induced hemorrhagic shock by removing a sufficient quantity of blood to maintain a mean arterial pressure of 50 mm Hg or less for 120 min. The animals were then resuscitated with shed blood and an equal volume of 0.9% saline. The experimental group received 10,000 units of IL-10 at the initiation of shock. Serum IL-1, IL-6, TNF, and lactate were

measured at baseline, after 120 min of shock, and 60 min after resuscitation. The rats were followed for 72 h to calculate survival.

RESULTS: Similar levels of hypoperfusion were obtained in both groups as

demonstrated by lactate levels and amount of shed blood. The survival rate (70%) was the same in both groups.

Serum levels of

IL-1 and IL-6 were not significantly different between the two groups, although there was a trend toward IL-6 suppression. TNF, however, was significantly lower in the IL-10-treated group at the end of shock (Wilcoxon test, $P < 0.025$).

CONCLUSION: Administration of IL-10 suppresses the TNF surge observed after severe hemorrhagic shock.

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L6 ANSWER 10 OF 43 MEDLINE
DUPLICATE 9

ACCESSION NUMBER: 2000130974

MEDLINE

DOCUMENT NUMBER: 20130974

PubMed ID: 10663839

TITLE: Serum cytokine profile in reflux nephropathy.

AUTHOR: Jutley R S; Youngson G G; Eremin O; Ninan G K

CORPORATE SOURCE: Department of Surgery, University of Aberdeen Medical School, Foresterhill Hospital, Aberdeen, AB9 2ZG, UK.

SOURCE: PEDIATRIC SURGERY INTERNATIONAL, (2000) 16 (1-2) 64-8.

Journal code: 8609169. ISSN: 0179-0358.

PUB. COUNTRY: GERMANY: Germany, Federal Republic of

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200003

ENTRY DATE: Entered STN: 20000320

Last Updated on STN:

20000320

Entered Medline: 20000307

AB Cytokines are small regulatory peptides with diverse functions. They

regulate the immune system and modulate the inflammatory response, both of which are implicated in vesico-ureteric reflux (VUR) and associated reflux nephropathy (RN). The cytokine profile in VUR and RN has yet to be fully

investigated. Blood was obtained from three subject groups immediately

after induction of anaesthesia: group A [subjects with VUR and established

RN, (N=9)]; group B [VUR alone but no associated RN, (N=6)]; and group C

[age- and sex-matched controls with no history of urinary sepsis

, (N=14)]. Serum cytokine levels of tumour-necrosis factor-alpha

(TNF-alpha), interleukin-6 (IL-6), soluble TNF

receptor-1 (sTNF-R1), and interleukin-8 (IL-8) were measured using

standard ELISA technique. Serum levels of IL-6 were

higher in group A subjects (1.798-4.638 pg/ml, median 3.253 pg/ml) than

controls (1.531-2.078 pg/ml, median 1.798 pg/ml). There was no significant

difference in levels in group B subjects (1.498-3.048 pg/ml, median 1.948

pg/ml) and controls. These same

relationships were observed for levels of

TNF-alpha (group A: 8.501-14.471

pg/ml, median 13.483 pg/ml; group B:

7.088-10.650 pg/ml, median 8.886 pg/ml;

group C: 6.746-13.344 pg/ml,

median 7.671 pg/ml) and sTNF-R1

(group A: 690.34-5780.74 pg/ml, median

1197.38 pg/ml; group B: 366.65-1401.62

pg/ml, median 592.82 pg/ml; C:

313.49-636.33 pg/ml, median 504.17

pg/ml). IL-8 was not significantly

elevated in any of the study groups (A or

B) compared with control group C

(group A: 27.08-56.38 pg/ml, median

31.35 pg/ml; group B: 29.90-35.87

pg/ml, median 31.35 pg/ml; group C:

25.05-30.22 pg/ml, median 29.90

pg/ml). These results suggest there may be an immunological basis to RN.

L6 ANSWER 11 OF 43 MEDLINE
DUPLICATE 10

ACCESSION NUMBER: 2001326645

MEDLINE

DOCUMENT NUMBER: 21288463

PubMed ID: 11394228

TITLE: [Interleukin-6, procalcitonin, C-reactive protein and the immature to total neutrophil ratio (I/T) in the diagnosis of early-onset sepsis in low birth weight neonates].

Interleukin-6, procalcitonin, C-reaktivni protein a pomer I/T v diagnostice casne sepse u novorozencu nizke porodni hmotnosti.

AUTHOR: Janota J; Stranak Z; Belohlavkova S

CORPORATE SOURCE: Ustav pro peci o matku a dite, Praha.

SOURCE: CESKA GYNEKOLOGIE, (2000 Dec) 65 Suppl 1 29-33.

Journal code: 9423768. ISSN: 1210-7832.

PUB. COUNTRY: Czech Republic

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: Czech

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200107

ENTRY DATE: Entered STN:

20010709

Last Updated on STN:

20010709

Entered Medline: 20010705

AB OBJECTIVE: To determine the influence of early-onset neonatal sepsis on interleukin-6 (IL-6) and procalcitonin (PCT) levels in cord blood.

To evaluate the significance of usually used infection markers--C-reactive protein (CRP) and immature to total neutrophil ratio (I/T)--and new markers (PCT, IL-6) for the diagnosis of early-onset neonatal sepsis.

DESIGN: Prospective clinical study. SETTING: Institute for the Care of Mother and Child, Prague. METHODS: The serum levels of IL-6 and PCT were

measured in cord blood in 37 low birth weight infants less than 35 week of gestation born in our institute. IL-6 and PCT levels were further evaluated together with CRP and I/T in neonatal blood within 2 hours after delivery. Neonatal sepsis within the first 72 hours of life was

monitored. RESULTS: Differences in mean values of CRP, I/T, IL-6, and PCT

between "sepsis proven" and "sepsis not proven" groups

were not statistically significant. Only the difference between groups in

cord blood PCT was of borderline

significance ($p = 0.06$, higher in "

sepsis proven" group). Fisher test

showed significant dependence

on sepsis in cord blood PCT only (cut-off point 0.4 ng/ml, $p <$

or $= 0.05$). Other parameters did not show significant dependence on

sepsis. Sensitivity for early onset sepsis above 50% was

found in cord blood PCT only (sensitivity 60%, specificity 85.2%). PCT

predictive accuracy for sepsis expressed as AUC value was 0.74

+/- 0.06. CONCLUSION: The only relatively sensitive marker and moderate predictor of early-onset sepsis in premature low birthweight infant was in our study cord blood PCT.

L6 ANSWER 12 OF 43 MEDLINE
DUPLICATE 11

ACCESSION NUMBER: 2000014237
MEDLINE

DOCUMENT NUMBER: 20014237
PubMed ID: 10548201

TITLE: Discrimination of infectious and noninfectious causes of early acute respiratory distress syndrome by procalcitonin.

COMMENT: Comment in: Crit Care Med. 1999 Oct;27(10):2304-5

AUTHOR: Brunkhorst F M; Eberhard O K; Brunkhorst R

CORPORATE SOURCE: Department of Intensive Care Medicine, Neukolln Teaching Hospital, Berlin, Germany.

SOURCE: CRITICAL CARE MEDICINE, (1999 Oct) 27 (10) 2172-6.
Journal code: 0355501. ISSN:

0090-3493.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals

ENTRY MONTH: 199911

ENTRY DATE: Entered STN:

20000111

Last Updated on STN:

20000111

Entered Medline: 19991116
AB OBJECTIVE: To test the sepsis marker procalcitonin (PCT) for its applicability to discriminate between septic and nonseptic causes of acute respiratory distress syndrome (ARDS).
DESIGN: Prospective study, assessing the course of PCT serum levels in early (within 72 hrs after onset) ARDS. The three other inflammation markers neopterin, interleukin-6 (IL-6), and C-reactive protein (CRP) were tested in parallel. SETTING: Twenty-four-bed medical intensive care unit of a 1,990-bed primary hospital, providing health care for an estimated 39,000 patients. PATIENTS: Twenty-seven patients, 18 male and nine female, aged 16-85 yrs, with early ARDS of known cause (17 with septic and ten with nonseptic ARDS) were enrolled in a prospective study between May 1994 and May 1995. INTERVENTIONS: Serum samples were drawn every 4-6 hrs for measurement of PCT, neopterin, IL-6, and CRP concentrations. Blood cultures, tracheal aspirates, and urine samples were obtained every 12-24 hrs. In 24 of 27 patients, bronchoscopic cultures were also obtained. Clinical sepsis criteria as defined by the American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference were checked daily. MEASUREMENTS AND MAIN RESULTS: Assessment of inflammation marker serum levels in septic vs. nonseptic ARDS. PCT serum levels were significantly higher ($p < .0005$) in the patients with septic ARDS than in patients with nonseptic ARDS within 72 hrs after onset of ARDS. There was no overlap between the two groups. Also, neopterin allowed a differentiation ($p < .005$), although a substantial overlap between serum levels of septic and nonseptic patients was observed. No discrimination could be achieved by determination of CRP and IL-6 levels. CONCLUSION: PCT determination in early ARDS could help to discriminate

between septic and nonseptic underlying disease.

L6 ANSWER 13 OF 43 MEDLINE
DUPLICATE 12
ACCESSION NUMBER: 1999253575
MEDLINE
DOCUMENT NUMBER: 99253575
PubMed ID: 10321658
TITLE: Effects of ibuprofen on the physiology and survival of hypothermic sepsis. Ibuprofen in Sepsis Study Group.
COMMENT: Comment in: Crit Care Med. 1999 Apr;27(4):669-70
AUTHOR: Arons M M; Wheeler A P; Bernard G R; Christman B W; Russell J A; Schein R; Sumner W R; Steinberg K P; Fulkerson W; Wright P; Dupont W D; Swindell B B
CORPORATE SOURCE: Department of Medicine, Vanderbilt University School of Medicine, Nashville, TN, USA.
CONTRACT NUMBER: HL 07123 (NHLBI) HL 19153 (NHLBI) HL 43167 (NHLBI)
SOURCE: CRITICAL CARE MEDICINE, (1999 Apr) 27 (4) 699-707.
Journal code: 0355501. ISSN: 0090-3493.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL) Journal; Article; (JOURNAL ARTICLE) (MULTICENTER STUDY) (RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199905
ENTRY DATE: Entered STN: 19990607
Last Updated on STN: 19990607
Entered Medline: 19990526
AB OBJECTIVES: The objective was to compare the clinical and physiologic characteristics of febrile septic patients with hypothermic septic patients; and to examine plasma levels of cytokines tumor necrosis factor alpha (TNF-alpha and interleukin 6 (IL-6) and the

lipid mediators thromboxane B2 (TxB2) and prostacyclin in hypothermic septic patients in comparison with febrile patients. Most importantly, we wanted to report the effect of ibuprofen treatment on vital signs, organ failure, and mortality in hypothermic sepsis. SETTING: The study was performed in the intensive care units (ICUs) of seven clinical centers in the United States and Canada.

PATIENTS: Four hundred fifty-five patients admitted to the ICU who met defined criteria for severe sepsis and were suspected of having a serious infection.

INTERVENTION: Ibuprofen at a dose of 10 mg/kg (maximum 800 mg) was administered intravenously over 30 to 60 mins every 6 hrs for eight doses vs. placebo (glycine buffer vehicle).

MEASUREMENTS AND MAIN RESULTS: Forty-four (10%) septic patients met criteria for hypothermia and 409 were febrile. The mortality rate was significantly higher in hypothermic patients, 70% vs. 35% for febrile patients.

At study entry, urinary metabolites of TxB2, prostacyclin, and serum levels of

TNF-alpha and IL-6 were significantly elevated in hypothermic patients compared with febrile patients. In hypothermic patients treated with ibuprofen, there was a trend toward an increased number of days free of major organ system failures and a significant reduction in the 30-day mortality rate from 90% (18/20 placebo-treated patients) to 54% (13/24 ibuprofen-treated patients).

CONCLUSIONS: Hypothermic sepsis has an incidence of approximately 10% and an untreated mortality twice that of severe sepsis presenting with fever. When compared with febrile patients, the hypothermic group has an amplified response with respect to cytokines TNF-alpha and IL-6 and lipid mediators TxB2 and prostacyclin.

Treatment with ibuprofen may decrease mortality in this select group of septic patients.

L6 ANSWER 14 OF 43 MEDLINE
DUPLICATE 13

ACCESSION NUMBER: 1999426669

MEDLINE

DOCUMENT NUMBER: 99426669

PubMed ID: 10498355

TITLE: Dynamic profiles of interleukin-6 and the soluble form of CD25 in burned patients.

AUTHOR: Peteiro-Cartelle F J; Alvarez-Jorge A

CORPORATE SOURCE: Laboratories, Juan Canalejo Hospital, La Coruna, Spain.

SOURCE: BURNS, (1999 Sep) 25 (6) 487-91.

Journal code: 8913178. ISSN:

0305-4179.

PUB. COUNTRY: ENGLAND: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199911

ENTRY DATE: Entered STN: 20000111

Last Updated on STN:

20000111

Entered Medline: 19991103

AB Changes in the time courses of serum levels of

interleukin-6 (IL6) and the soluble form of CD25 (sCD25)

were evaluated in 48 burned patients (31 had sepsis, 21 died).

Differences among groups along the time were assessed with ANOVA. The

Pearson's r correlation coefficient was used to relate quantitative

variables. ROC curves were constructed to analyse the prognostic value of

IL6 and sCD25. The values of IL6 and sCD25 were related to treatment

outcome and time post-burn. In general, two patterns emerged: In

non-survivors, there was a depression of sCD25 with time, and an increase

in IL6 levels previous to death, whereas survivors had the opposite

pattern. On admission, patients with higher levels of sCD25 had a bad prognosis.

L6 ANSWER 15 OF 43 MEDLINE

DUPLICATE 14

ACCESSION NUMBER: 1999223068
MEDLINE

DOCUMENT NUMBER: 99223068
PubMed ID: 10208387
TITLE: Changes in circulating levels
of interleukin 6 in burned
patients.

AUTHOR: Yeh F L; Lin W L; Shen H
D; Fang R H

CORPORATE SOURCE: Department of
Surgery, Veterans General Hospital-Taipei
and

National Yang-Ming University,
Taiwan.

SOURCE: BURNS, (1999 Mar) 25
(2) 131-6.

Journal code: 8913178. ISSN:
0305-4179.

PUB. COUNTRY: ENGLAND: United
Kingdom

DOCUMENT TYPE: Journal; Article;
(JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199906

ENTRY DATE: Entered STN:
19990618

Last Updated on STN:
19990618

Entered Medline: 19990607
AB Interleukin 6 (IL-6) levels in serial
serum samples of

10 burned patients were analyzed. The
total body surface areas (TBSA) of
the burn injury varied from 30 to 85%.
Among these 10 patients, five
recovered and the other five, who were
septic, expired. A significant
difference in serum IL-6 values on
admission (5-13 h postburn) was found
($p < 0.05$) between patients who survived
or died from burn injury as

analyzed by the Wilcoxon's rank sum
test. In addition, a significant
difference in serum IL-6 on admission
was also found ($p < 0.05$) between
patients with TBSA of greater or less
than 50%. Afterwards, an initial
peak serum IL-6 response was detected
within 4 days postburn. Significant
differences in the peak serum IL-6 levels
were not found between patients
with TBSA of greater or less than 50%
and patients who survived or expired
from burn injury. In the survivors, serum
IL-6 remained low, while IL-6
increased markedly starting at about one
to two weeks postburn in four of

the five nonsurvivors with proven sepsis.
Except for the patient
who expired 42 days postburn, the
maximum serum IL-6 values of the other
four nonsurvivors were all greater than
those of the five survivors from
burn injury. Significant correlation ($p < 0.05$) relating the change in
serum IL-6 and body temperature was
observed in only two (one survivor and
one nonsurvivor) of the ten patients.
Changes in serum IL-6 were also
compared with changes in circulating
TNF-alpha and IL-8 determined
previously. A similar pattern in the
dynamic changes of circulating
TNF-alpha, IL-8 and IL-6 was observed
in the individual burned patient. An
increase in serum levels of all three
cytokines was
detected postburn. Serum levels of three
cytokines
were significantly higher in the septic
patients, who all died. It was
considered that all three cytokines
analyzed may play a significant role
in the pathophysiology of sepsis in
burned patients.

L6 ANSWER 16 OF 43 MEDLINE
DUPLICATE 15
ACCESSION NUMBER: 1998315686
MEDLINE
DOCUMENT NUMBER: 98315686
PubMed ID: 9618243
TITLE: Endotoxin and tumor
necrosis factor alpha exert a similar
proinflammatory effect in
neonatal rat cardiomyocytes, but
have different cardiodepressant
profiles.

AUTHOR: Muller-Werdan U;
Schumann H; Loppnow H; Fuchs R; Darmer
D;

Stadler J; Holtz J; Werdan K
CORPORATE SOURCE: Department of
Medicine III, Klinikum Krollwitz, University
of Halle-Wittenberg, Germany.

SOURCE: JOURNAL OF
MOLECULAR AND CELLULAR
CARDIOLOGY, (1998 May) 30
(5) 1027-36.

Journal code: 0262322. ISSN:
0022-2828.

PUB. COUNTRY: ENGLAND: United
Kingdom

DOCUMENT TYPE: Journal; Article;
(JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199809

ENTRY DATE: Entered STN:

19980925

Last Updated on STN:

19980925

Entered Medline: 19980917

AB Bolus application of endotoxin to healthy volunteers results in reversible hemodynamic alterations, such as observed in septic cardiomyopathy.

Currently, endotoxin-induced cardiodepression is mainly attributed to the endotoxin-induced release of proinflammatory cytokines into the circulation, particularly of tumor necrosis factor alpha and

interleukin-1, the serum levels of these cytokines

being enhanced in sepsis and septic shock, and also in various heart diseases. In this study, we report a proinflammatory effect of

endotoxin (1-10 micrograms/ml, 24-h incubation period) on neonatal rat

cardiomyocytes in serum-free culture, evidenced by induction of inducible nitric oxide synthase, enhanced release of nitrite (protein

synthesis-dependent) and interleukin-6 into the

supernatant, as well as an increase in cell-associated interleukin-1 and a

specific cardiodepressant profile: endotoxin disrupts beta-adrenoceptor-mediated increase in pulsation amplitude,

but alpha-adrenoceptor-induced increase in pulsation amplitude and arrhythmias are not suppressed. In the

presence of dexamethasone (0.1 microM), the endotoxin-mediated blockade of

beta-adrenergic responsiveness, as well as induction of inducible nitric

oxide synthase, enhanced nitrite release and interleukin-1/-6-production

are inhibited. In contrast, tumor necrosis factor alpha at a low

concentration (10 U/ml) depresses alpha- and beta-adrenergic

responsiveness in the presence of dexamethasone in a nitric

oxide-independent manner. These data suggest a stimulatory effect of endotoxin on the cardiomyocyte and a specific proinflammatory and nitric oxide-dependent cardiodepressant profile of endotoxin.

L6 ANSWER 17 OF 43 MEDLINE

DUPLICATE 16

ACCESSION NUMBER: 1998260348

MEDLINE

DOCUMENT NUMBER: 98260348

PubMed ID: 9580629

TITLE: Modulation of mouse endotoxin shock by inhibition of phosphatidylcholine-specific phospholipase C.

AUTHOR: Tschaikowsky K; Schmidt J; Meisner M

CORPORATE SOURCE: Department of Anesthesiology, University of Erlangen-Nurnberg, Germany..

klaus.tschaikowsky@rzmail.uni-erlangen.de

SOURCE: JOURNAL OF PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS,

(1998 May) 285 (2) 800-4.

Journal code: 0376362. ISSN:

0022-3565.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article;
(JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199806

ENTRY DATE: Entered STN:

19980618

Last Updated on STN:

19990129

Entered Medline: 19980608

AB During Gram-negative bacterial infections, lipopolysaccharide (LPS) interacts with monocyte/macrophage receptors, resulting in a host defense response. Activation of intracellular signal transduction pathways

implicating various protein kinase and phospholipases is crucial in

activating the transcription of genes encoding proinflammatory cytokines

and inducible nitric oxide synthase (iNOS). In this article, we

demonstrate that in mouse, endotoxin shock activation of

phosphatidylcholine-specific
phospholipase C (PC-PLC) plays a major
role
in controlling the inflammatory response.
Inhibition of PC-PLC by the
specific inhibitor tricyclodecan-9-yl-
xanthogenate (D609) before LPS
reduced the release of interleukin-1 beta,
interleukin-6
and nitric oxide (NO) in vivo. In contrast,
tumor necrosis factor-alpha
serum levels were not altered by the
pretreatment with
D609. Consequently, survival from
endotoxin shock of D609-treated animals
was significantly improved compared with
control animals (45% vs. 20%).
Thus, inhibition of PC-PLC can reduce
the inflammatory response to LPS and
may serve as a novel approach to
therapy of sepsis.

L6 ANSWER 18 OF 43 MEDLINE
DUPLICATE 17
ACCESSION NUMBER: 1999068697
MEDLINE
DOCUMENT NUMBER: 99068697
PubMed ID: 9853808
TITLE: Validation of an automated
enzyme immunoassay for
Interleukin-6 for routine clinical
use.
AUTHOR: Fraunberger P; Pfeiffer M;
Cremer P; Holler E; Nagel D;
Dehart I; Thein M; Walli A K;
Seidel D
CORPORATE SOURCE: Institut fur
Klinische Chemie, Klinikum Grosshadern,
LMU
Munchen, Munich, Germany.
SOURCE: CLINICAL CHEMISTRY
AND LABORATORY MEDICINE, (1998.Oct)
36
(10) 797-801.
Journal code: 9806306. ISSN:
1434-6621.
PUB. COUNTRY: GERMANY: Germany,
Federal Republic of
DOCUMENT TYPE: Journal; Article;
(JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199902
ENTRY DATE: Entered STN:
19990301

Last Updated on STN:
19990301
Entered Medline: 19990212
AB Serum levels of Interleukin-6
(IL-6), a proinflammatory cytokine, are
increased in early stages of
inflammatory diseases such as infection
and sepsis. Assay
systems which permit its measurement
within a few hours and as a single
measurement have not been reported so
far. We therefore evaluated a now
commercially available automated
method for IL-6 measurement on the Cobas
Core immunological analyzer (Roche
Diagnostic Systems) which enables
single IL-6 measurement within about 1
hour. The automated assay
correlates well with an established,
manual microtiter plate assay
(Biosource GmbH) which uses the same
antibodies and reagents ($r=0.98$).
Accuracy of the automated method was
established by adding known amounts
of IL-6 international reference
preparation. Recovery of the international
standard was in the range of 92-104%.
The automated assay had a precision
of singletons below 6% and was linear up
to 2800 pg/ml. This automated
assay provides a suitable, convenient
and time saving method for
measurement of IL-6 serum levels in the
routine
clinical laboratory.

L6 ANSWER 19 OF 43 CAPLUS
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ACCESSION NUMBER: 1998:69548
CAPLUS
DOCUMENT NUMBER: 128:152980
TITLE: The dual role of
interferon-gamma. in experimental
Staphylococcus aureus
septicemia versus arthritis
AUTHOR(S): Zhao, Y.-X.; Nilsson,
I.-M.; Tarkowski, A.
CORPORATE SOURCE: Departments
Rheumatology Clinical Immunology,
University Goteborg,
Goteborg, Swed.
SOURCE: Immunology (1998),
93(1), 80-85
CODEN: IMMUAM; ISSN:
0019-2805

PUBLISHER: Blackwell Science Ltd.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB To evaluate the role of interferon- γ . (IFN- γ .) in Staphylococcus aureus infection, the authors investigated the effects of supplementation with and neutralization of IFN- γ . during septicemia and arthritis in a murine model. In vivo administration of IFN- γ . both before and after bacterial inoculation significantly decreased mortality on one hand but enhanced the development of arthritis on the other. Treatment of mice with anti-IFN- γ . monoclonal antibodies (mAb) before and after bacterial inoculation did not significantly influence the survival rate but decreased the frequency and severity of arthritis. The beneficial effect of supplementation with IFN- γ . on septicemia was correlated to the increased phagocytosis and bacterial clearance from liver and kidneys. The down-regulation of the development of arthritis by anti-IFN- γ . mAb was accompanied by the decreased serum tumor necrosis factor α ., interleukin-6 and interleukin-1 β . levels. These results demonstrate a significant role for IFN- γ . in simultaneous protection against septicemia but promotion for the development of septic arthritis.

L6 ANSWER 20 OF 43 MEDLINE
 DUPLICATE 18

ACCESSION NUMBER: 97413373

MEDLINE

DOCUMENT NUMBER: 97413373

PubMed ID: 9269788

TITLE: Downregulation of the proinflammatory cytokine response to endotoxin by pretreatment with the nontoxic lipid A analog SDZ MRL 953 in cancer patients.

AUTHOR: Kiani A; Tschiersch A; Gaboriau E; Otto F; Seiz A; Knopf H P; Stutz P; Farber L; Haus U; Galanos C; Mertelsmann R; Engelhardt R

CORPORATE SOURCE: Department of Internal Medicine I, University Hospital of

Freiburg, Germany.

SOURCE: BLOOD, (1997 Aug 15)
 90 (4) 1673-83.

Journal code: 7603509. ISSN: 0006-4971.

PUB. COUNTRY: United States

DOCUMENT TYPE: (CLINICAL TRIAL)
 (CLINICAL TRIAL, PHASE I)
 Journal; Article; (JOURNAL

ARTICLE)
 (RANDOMIZED CONTROLLED TRIAL)

LANGUAGE: English

FILE SEGMENT: Abridged Index

Medicus Journals; Priority Journals

ENTRY MONTH: 199709

ENTRY DATE: Entered STN:
 19971008

Last Updated on STN:
 19971008

Entered Medline: 19970924
 AB Interfering with the endotoxin-mediated cytokine cascade is thought to be a promising approach to prevent septic complications in gram-negative infections. The synthetic lipid A analog SDZ MRL 953 has been shown to be protective against endotoxic shock and bacterial infection in preclinical in vivo models. As part of a trial of unspecific immunostimulation in cancer patients, we conducted a double-blind, randomized, vehicle-controlled phase I trial of SDZ MRL 953 to investigate, first, its biologic effects and safety of administration in humans and, second, its influence on reactions to a subsequent challenge of endotoxin (Salmonella abortus equi). Twenty patients were treated intravenously with escalating doses of SDZ MRL 953 or vehicle control, followed by an intravenous application of endotoxin (2 ng/kg of body weight [BW]). Administration of SDZ MRL 953 was safe and well-tolerated. SDZ MRL 953 itself increased granulocyte counts and serum levels of granulocyte colony-stimulating factor (G-CSF) and interleukin-6 (IL-6), but not of the proinflammatory cytokines tumor necrosis factor- α (TNF- α), IL-1 β , and IL-8. Compared with vehicle

control, pretreatment with SDZ MRL 953 markedly reduced the release of TNF-alpha, IL-1beta, IL-8, IL-6, and G-CSF, but augmented the increase in granulocyte counts to endotoxin. Induction of tolerance to the endotoxin-mediated cascade of proinflammatory cytokines by pretreatment with SDZ MRL 953 in patients at risk may help to prevent complications of gram-negative sepsis.

L6 ANSWER 21 OF 43 MEDLINE
DUPLICATE 19
ACCESSION NUMBER: 1998010367
MEDLINE
DOCUMENT NUMBER: 98010367
PubMed ID: 9350884
TITLE: Interleukin 6, but not tumour necrosis factor-alpha, is a good predictor of severe infection in febrile neutropenic and non-neutropenic children with malignancy.
AUTHOR: Abrahamsson J; Pahlman M; Mellander L
CORPORATE SOURCE: Department of Pediatrics, University of Goteborg, Sweden.
SOURCE: ACTA PAEDIATRICA, (1997 Oct) 86 (10) 1059-64.
Journal code: 9205968. ISSN: 0803-5253.
PUB. COUNTRY: Norway
DOCUMENT TYPE: Journal; Article;
(JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199711
ENTRY DATE: Entered STN:
19971224

Last Updated on STN:
19971224
Entered Medline: 19971119
AB OBJECTIVE: Interleukin-6 (IL6), tumor necrosis factor-alpha (TNF-alpha) and interferon-gamma (IFN-gamma) are important mediators of the inflammatory response in human infection. The aim of this study was to determine the relationship between serum levels of IL6, TNF-alpha, IFN-gamma and CRP in febrile children with malignant disease, and relate these levels to aetiology of fever,

presence of neutropenia and the effect of untreated malignancy. METHODS:

110 febrile episodes in 70 children with malignant disease were included.

Cytokine analyses were performed with sensitive immunoradiometric methods using double monoclonal antibodies.

RESULTS: IL6 had a sensitivity of 74% in detecting sepsis in children with fever and malignant

disease. This sensitivity was not influenced by the presence of neutropenia or newly diagnosed malignancy. A positive correlation between IL6 and the CRP levels on the following day was observed ($r = .53$).

TNF-alpha was elevated in 22% of the episodes and mean levels were significantly higher in untreated malignancy but lower in neutropenic patients. IFN-gamma was elevated in 18% of cases and correlated strongly with mean TNF-alpha levels.

CONCLUSIONS: IL6 is a sensitive and early predictor of bacterial infection in both neutropenic and non-neutropenic febrile children with malignancy. It is more sensitive than CRP in detecting sepsis, but the predictive value is too low to allow

IL6 levels to influence initial treatment decisions in patients with granulocytopenia. TNF-alpha production seems to be impaired in neutropenic children and serum TNF-alpha cannot be employed as an indicator of bacterial infection.

L6 ANSWER 22 OF 43 MEDLINE
DUPLICATE 20
ACCESSION NUMBER: 97276938
MEDLINE
DOCUMENT NUMBER: 97276938
PubMed ID: 9130631
TITLE: Superantigen and endotoxin synergize in the induction of lethal shock.
AUTHOR: Blank C; Luz A; Bendigs S; Erdmann A; Wagner H; Heeg K
CORPORATE SOURCE: Institute of Medical Microbiology, Immunology and Hygiene,
Munich, Germany.
SOURCE: EUROPEAN JOURNAL OF IMMUNOLOGY, (1997 Apr) 27 (4) 825-33.

Journal code: 1273201. ISSN:
0014-2980.

PUB. COUNTRY: GERMANY: Germany,
Federal Republic of

DOCUMENT TYPE: Journal; Article;
(JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199705

ENTRY DATE: Entered STN:
19970602

Last Updated on STN:
19970602

Entered Medline: 19970522
AB Endotoxin (lipopolysaccharide; LPS)

and superantigens (exotoxins) have
been identified as potent inducers of
lethal shock. While endotoxin
primarily interacts with CD14 receptors
on macrophages, superantigens like
the staphylococcal enterotoxin B (SEB)
preferentially activate T cells.

Both cell types are triggered to release
pro-inflammatory cytokines that
in turn induce lethal shock. We analyzed
whether endotoxin and

superantigen interact during the induction
phase of lethal shock. We

report that LPS and SEB operate
synergistically. Lethal doses of both
inducers were reduced 100-fold when
given in combination. The induced
serum levels of tumor necrosis factor,
interleukin-6, and interferon-gamma (IFN-
gamma) were

elevated and remained high for a
prolonged period. Moreover, synergistic
action of LPS and SEB induced lethal
toxic shock even without

presensitization of mice with D-
galactosamine (D-GalN). Opposed to

D-GalN-pretreated mice, mice injected
with LPS and SEB showed less liver
damage, but rather apoptosis of epithelial
cells in the bowel. Cyclosporin

A and treatment with anti-IFN-gamma
monoclonal antibody blocked the
synergistic action of LPS and SEB,
indicating that T cell-derived

IFN-gamma is the mediator of the
observed synergism. Concomitant injection
of LPS and SEB had no influence on
SEB-induced T cell deletion and anergy
induction. Since Gram-positive and
Gram-negative bacteria can be recovered

from septic blood samples, the
synergistic action of endotoxin and
superantigens might be relevant during
lethal septicemia.

L6 ANSWER 23 OF 43 CAPLUS

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ACCESSION NUMBER: 1997:621821
CAPLUS

DOCUMENT NUMBER: 127:276994
TITLE: Immunological status of

septic and trauma patients. I.

High tumor necrosis factor
.alpha. serum levels in

septic and trauma patients
are not responsible for

increased mortality; a
prognostic value of serum

interleukin 6

AUTHOR(S): Adamik, Barbara;
Zimecki, Michal; Wlaszczyk, Andrzej;

Kubler, Andrzej

CORPORATE SOURCE: Department of
Anesthesiology and Intensive Therapy,

University Medical School,
Wroclaw, 50-368, Pol.

SOURCE: Archivum
Immunologiae et Therapiae Experimentalis
(1997), 45(2-3), 169-175

CODEN: AITEAT; ISSN:

0004-069X

PUBLISHER: Zaklad Narodowy
imienia Ossolinskich

DOCUMENT TYPE: Journal
LANGUAGE: English

AB The aim of this study was to monitor
plasma interleukin 6 (IL-6), and

tumor necrosis factor .alpha. (TNF-
.alpha.), levels in patients with

sepsis, septic shock and multiple organ
dysfunction syndrome admitted to

the intensive care unit. The patients
obtained adequate supportive

therapy. Plasma samples were taken
upon admission, then on days 1, 2, and

5 following admission. IL-6 and TNF-
.alpha. levels were detd. using

bioassays (7TD1 and WEHI-164.13
indicator cell lines, resp.). The results

showed that the kinetics of the cytokine
release in septic patients

differed significantly between survivors
and non-survivors. In survivors

IL-6 concns. were initially high, fell down
rapidly on day 1 after

admission, and persisted very low throughout the monitoring time. In contrast, relatively low IL-6 levels in the non-survivors, registered upon admission, rose significantly with peak values on day 3 of observation, declining thereafter. TNF-.alpha. levels were initially higher in survivors than in non-survivors, declined on day 1 following admission, and on day 5 they were higher than the initial values. In non-survivors, the starting concns. of TNF-.alpha. were much lower than in survivors with a peak on day 3 with a tendency to fall on day 7. The profiles of cytokine prodn. by traumatic patients (90% survivors) revealed low and progressively diminishing levels of IL-6, contrasting with constantly increasing concns. of TNF-.alpha. within the monitoring period. The authors conclude that high IL-6 levels in septic patients accompanied by high TNF-.alpha. levels may indicate bad prognosis. In contrast, rapidly diminishing serum IL-6 levels, even in the presence of high TNF-.alpha. levels, could indicate a very good chance for survival. Similar conclusion can be drawn from the monitoring of cytokine prodn. in traumatic, non-septic patients since almost all of them recovered. The authors also speculate that TNF-.alpha. presence in circulating blood is essential for regeneration of tissues and wound healing.

L6 ANSWER 24 OF 43 MEDLINE
DUPLICATE 21

ACCESSION NUMBER: 97211299

MEDLINE

DOCUMENT NUMBER: 97211299

PubMed ID: 9058297

TITLE: Hepatocyte growth factor in
assessment of acute
pancreatitis: comparison with C-
reactive protein and
interleukin-6.

AUTHOR: Ueda T; Takeyama Y;
Hori Y; Nishikawa J; Yamamoto M; Saitoh
Y

CORPORATE SOURCE: First Department
of Surgery, Kobe University School of
Medicine, Japan.

SOURCE: JOURNAL OF
GASTROENTEROLOGY, (1997 Feb) 32 (1)
63-70.

Journal code: 9430794. ISSN:

0944-1174.

PUB. COUNTRY: Japan

DOCUMENT TYPE: Journal; Article;
(JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199705

ENTRY DATE: Entered STN:
19970609

Last Updated on STN:

19970609

Entered Medline: 19970523

AB Serum levels of hepatocyte growth
factor (HGF),

C-reactive protein (CRP), and interleukin-
6 (IL-6)

were determined at the time of admission
in 38 patients with acute

pancreatitis. The clinical utility of HGF for
the detection of severe

pancreatitis and for predicting prognosis,
bacterial infection (infected

pancreatic necrosis or sepsis), and organ
dysfunction (liver,

kidney, and lung) during the clinical
course of acute pancreatitis was

compared with the clinical utility of CRP
and IL-6 by analysis of receiver

operator characteristic (ROC) curves.
The optimum cutoff levels of HGF for

severity, prognosis, infection, hepatic
dysfunction, renal dysfunction,

and respiratory dysfunction were 0.9, 1.1,
1.0, 1.1, 1.1, and 1.0 ng/ml,

respectively. HGF was as useful as CRP
and more useful than IL-6 for

detection of severe pancreatitis and for
predicting hepatic dysfunction.

Moreover, HGF was more useful than
CRP or IL-6 for predicting prognosis,

renal dysfunction, and respiratory
dysfunction. However, for predicting

infection, CRP was more useful than
HGF. These results suggest that serum

HGF levels on admission may be a
useful new clinical parameter for

determining the prognosis of acute
pancreatitis and that HGF may be

closely related to the organ dysfunction
of acute pancreatitis.

L6 ANSWER 25 OF 43 MEDLINE
DUPLICATE 22

ACCESSION NUMBER: 97066033
MEDLINE

DOCUMENT NUMBER: 97066033
PubMed ID: 8909514

TITLE: High tumor necrosis factor
serum level is associated with
increased survival in patients
with abdominal septic shock:
a prospective study in 59

patients.

AUTHOR: Riche F; Panis Y; Laisne
M J; Briard C; Cholley B;

Bernard-Poenaru O; Graulet A
M; Gueris J; Valleur P

CORPORATE SOURCE: Department of
Anesthesiology, Lariboisiere Hospital, Paris,
France.

SOURCE: SURGERY, (1996 Nov)
120 (5) 801-7.

Journal code: 0417347. ISSN:
0039-6060.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article;
(JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Abridged Index
Medicus Journals; Priority Journals

ENTRY MONTH: 199612

ENTRY DATE: Entered STN:
19970128

Last Updated on STN:
19970128

Entered Medline: 19961213

AB BACKGROUND: In several studies
including patients with septic shock of
various origins, high serum cytokine
levels have been reported to
correlate with poor outcome. The aim of
this prospective study was to
assess the prognostic value of cytokine
serum levels

in a group of patients with perioperative
septic shock of digestive

origin. METHODS: From January 1992 to
December 1994, 59 patients were
evaluated (mean age, 68 +/- 15 years).

From the first day of septic shock
to day 7, blood was drawn every day to
measure the conventional biologic
parameters (white blood cell count,
platelet count, hematocrit, blood urea
nitrogen level, serum electrolytes level,
pH, blood gases, serum lactate

level, coagulation parameters, liver
function tests) and tumor necrosis
factor (TNF), interleukin-1, and
interleukin-6.

RESULTS: No difference was observed
between the 26 survivors and the 33
nonsurvivors with regard to age, gender,
and cause of sepsis. On

admission, mean platelet count was
significantly higher in the survivors

than in the nonsurvivors (260 +/- 142
versus 177 +/- 122 10(9)/L; p =

0.01). Mean blood urea nitrogen level
was significantly lower in the

survivors than in the nonsurvivors (9.6 +/-
9 versus 12 +/- 7 mmol/L; p =

0.04). No difference was observed
between survivors and nonsurvivors for
the other conventional biologic

parameters and for serum interleukin-1 and
interleukin-6 levels. Mean serum TNF
level tended to be

higher in survivors than in nonsurvivors
(565 +/- 1325 versus 94 +/- 69

pg/ml; not significant). In the group
survivor 9 (35%) of 26 patients had

a serum TNF level greater than 200
pg/ml versus 2 (6%) of 33 patients in

the nonsurvivor group (p < 0.02). Survival
was noted in 6 (100%) of 6

patients who had both a serum TNF level
greater than 200 pg/ml and a

platelet count greater than 100.10(9)/L
versus 1 (11%) of 9 in patients

with neither of these criteria (p < 0.01).

CONCLUSIONS: In our patients

with abdominal septic shock, high serum
TNF levels were associated with

increased survival. The high serum level
of TNF may reflect the efficacy

of peritoneal inflammatory response
against abdominal sepsis.

Although this possibility must be further
explored, a score combining the

serum TNF level and platelet count could
be helpful for the prognostic

assessment of patients with abdominal
septic shock.

L6 ANSWER 26 OF 43 MEDLINE
DUPLICATE 23

ACCESSION NUMBER: 96304180
MEDLINE

DOCUMENT NUMBER: 96304180
PubMed ID: 8753088

PATENT NO.	KIND	DATE	
APPLICATION NO.	DATE		
WO 9520978	A1	19950810	WO
1995-EP291		19950127	
W: AU, BR, BY, CA, CN, CZ, FI, HU, JP, KR, KZ, MX, NO, NZ, PL, RU, SI, UA, US			
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE			
DE 4409513	C1	19951019	DE
1994-4409513		19940319	
IL 112427	A1	19981206	IL
1995-112427		19950124	
CA 2182723	AA	19950810	CA
1995-2182723		19950127	
AU 9515201	A1	19950821	AU
1995-15201		19950127	
CN 1140414	A	19970115	CN
1995-191517		19950127	
JP 09509411	T2	19970922	JP
1995-520363		19950127	
BR 9506741	A	19971021	BR
1995-6741		19950127	
EP 804236	A1	19971105	EP
1995-906353		19950127	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI			
HU 76875	A2	19971229	HU
1996-2169		19950127	
TW 403656	B	20000901	TW
1995-84100744		19950127	
CZ 290843	B6	20021016	CZ
1996-2322		19950127	
ZA 9500956	A	19951011	ZA
1995-956		19950207	
FI 9603101	A	19960806	FI
1996-3101		19960806	
NO 9603280	A	19961004	NO
1996-3280		19960806	
MX 9603243	A	20000228	MX
1996-3243		19960807	
US 6235281	B1	20010522	US
1996-687328		19960807	
AU 9915495	A1	19990401	AU
1999-15495		19990208	
US 2001010819	A1	20010802	
US 2001-782290		20010214	
PRIORITY APPLN. INFO.:			DE
1994-4403669	A	19940207	
			DE 1994-4409513
A 19940319			
			AU 1995-15201
A3 19950127			

WO 1995-EP291

W 19950127

US 1996-687328

A1 19960807

AB Tumor necrosis factor (TNF) antagonists, esp. anti-TNF antibodies and their fragments, are useful in prodn. of drugs to treat diseases characterized by elevated interleukin-6 serum levels, e.g. sepsis.

L6 ANSWER 30 OF 43 MEDLINE
DUPLICATE 26
ACCESSION NUMBER: 96108305
MEDLINE
DOCUMENT NUMBER: 96108305
PubMed ID: 8658074
TITLE: High IL-6 serum levels are associated with septic shock and mortality in septic patients with severe leukopenia due to hematological malignancies.
AUTHOR: Antonelli M; Raponi G M; Martino P; Rosa G; Conti G; Jalouk J; Gasparetto A
CORPORATE SOURCE: Institute of Anesthesiology and Intensive Care, La Sapienza University of Rome, Italy.
SOURCE: SCANDINAVIAN JOURNAL OF INFECTIOUS DISEASES, (1995) 27 (4) 381-4.
Journal code: 0215333. ISSN: 0036-5548.
PUB. COUNTRY: Sweden
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199607
ENTRY DATE: Entered STN: 19960808
Last Updated on STN: 19980206
Entered Medline: 19960731
AB The serum levels of immunoreactive interleukin -6 (IL-6) and tumor necrosis factor (TNF) were analyzed in 14 leukopenic patients with documented sepsis, at 60 min (T0), 24 h (T1), and one week (T3) after the onset of sepsis syndrome. Sera

from 10 leukopenic patients without sepsis (controls) were also tested. All septic patients had high IL-6 levels at T0. These levels persisted only in the seven patients who died of septic shock, presenting a 30-fold increase ($p < 0.001$) as compared to the survivors and the controls. At T3, 7 survivors had recovered from sepsis and showed low IL-6 serum levels. The TNF serum concentration always < 30 pg/ml in both the subjects and in the controls. The C-reactive protein (CRP) and clinical parameters appeared to be less specifically associated with shock and mortality than IL-6.

L6 ANSWER 31 OF 43 MEDLINE
DUPLICATE 27

ACCESSION NUMBER: 95271638

MEDLINE

DOCUMENT NUMBER: 95271638

PubMed ID: 7752214

TITLE: Cytokine stimulation during
Salmonella typhimurium sepsis
in Itys mice.

AUTHOR: Jotwani R; Tanaka Y;
Watanabe K; Tanaka K; Kato N; Ueno K
CORPORATE SOURCE: Institute of
Anaerobic Bacteriology, Gifu University
School

of Medicine, Japan.

SOURCE: JOURNAL OF MEDICAL
MICROBIOLOGY, (1995 May) 42 (5) 348-
52.

Journal code: 0224131. ISSN:
0022-2615.

PUB. COUNTRY: SCOTLAND: United
Kingdom

DOCUMENT TYPE: Journal; Article;
(JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199506

ENTRY DATE: Entered STN:
19950629

Last Updated on STN:
19950629

Entered Medline: 19950622

AB Cytokine production was measured in mice during Salmonella typhimurium sepsis and intoxication. In mice given live S. typhimurium (10

cfu/mouse), by intra-peritoneal injection, serum levels

of tumour necrosis factor (TNF)-alpha and interleukin-6

increased steadily from day 1 until day 4.

Interferon-gamma levels showed

a transient peak on day 3. Interleukin-1-

alpha levels were very low. There

were high bacterial counts in the livers at day 3 and deaths occurred from

day 4 onwards. Intraperitoneal injection of lipopolysaccharide or

heat-killed bacteria also induced all of the cytokines, but their time of

appearance and levels varied greatly.

Cytokine induction by heat-killed

bacteria was more marked.

Endotoxaemia decreased with time during

intoxication and increased during sepsis.

Bioactive TNF, as

measured by a cytotoxicity assay, was

found only in mice given heat-killed bacteria.

L6 ANSWER 32 OF 43 MEDLINE
DUPLICATE 28

ACCESSION NUMBER: 95109670

MEDLINE

DOCUMENT NUMBER: 95109670

PubMed ID: 7810656

TITLE: Interleukin-6 inhibits
hepatocyte taurocholate uptake and
sodium-potassium-

adenosinetriphosphatase activity.

AUTHOR: Green R M; Whiting J F;

Rosenbluth A B; Beier D; Gollan J L

CORPORATE SOURCE: Division of
Gastroenterology, Brockton/West Roxbury
Veterans Affairs Medical

Center, Boston, Massachusetts.

CONTRACT NUMBER: DK-07533
(NIDDK)

DK-36887 (NIDDK)

SOURCE: AMERICAN JOURNAL
OF PHYSIOLOGY, (1994 Dec) 267 (6 Pt 1)
G1094-100.

Journal code: 0370511. ISSN:
0002-9513.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article;
(JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199501

ENTRY DATE: Entered STN:
19950215

Last Updated on STN:

19950215

Entered Medline: 19950131

AB The potential effects of cytokines on hepatocellular transport functions remain undefined. Interleukin-6 (IL-6) is a cytokine

that is produced in sepsis, hepatitis, and other inflammatory

conditions often associated with cholestasis. Using cultured rat

hepatocytes, we have investigated the effects of IL-6 on hepatocellular

bile salt uptake. Because hepatocyte Na(+)-K(+)-adenosinetriphosphatase

(ATPase) produces the electrochemical gradient that drives

sodium-dependent bile salt cotransport, we also examined the effects of

IL-6 on Na(+)-K(+)-ATPase activity.

Hepatocytes cultured for 20 h in media containing IL-6 exhibited a dose-

dependent noncompetitive inhibition of [3H]taurocholate uptake, which was maximal at an IL-6 dose of 100 U/ml.

IL-6 treatment had no effect on hepatocyte sodium-independent taurocholate

uptake. Northern blotting of RNA from cultured hepatocytes revealed that

IL-6 had no effect on steady-state RNA levels of the Na(+)-taurocholate

transporter (Ntcp). Hepatocytes

incubated with IL-6 for 20 h, however,

exhibited a 55% decrease in hepatocyte Na(+)-K(+)-ATPase activity. This

effect also was dose dependent, with maximal inhibition occurring at an

IL-6 dose of 100 U/ml. Similar treatment with IL-6 did not influence

hepatocyte Mg(2+)-ATPase activity. The inhibition of Na(+)-K(+)-ATPase

activity induced by IL-6 provides a putative mechanism for the observed

inhibition of sodium-dependent

taurocholate uptake. Since modulation of

bile salt transport and Na(+)-K(+)-

ATPase activity occurred at IL-6

concentrations comparable to the serum levels observed

in patients with severe inflammatory states, these findings have potential

pathophysiological relevance for the cholestasis of sepsis and

other inflammatory disorders.

L6 ANSWER 33 OF 43 CAPLUS

COPYRIGHT 2003 ACS DUPLICATE 29

ACCESSION NUMBER: 1995:474676

CAPLUS

DOCUMENT NUMBER: 122:237432

TITLE: Kinetics of serum levels of

interleukin-6 in

Staphylococcus

aureus septicemia

AUTHOR(S): Soederqvist, B.;

Sundqvist, K. -G.; Vikerfors, T.

CORPORATE SOURCE: Department Infectious Diseases, Orebro Medical Center

Hospital, Orebro, S-70185,

Swed.

SOURCE: Zentralblatt fuer

Bakteriologie, Supplement (1994),

26, 446-8

CODEN: ZBASE2; ISSN:

0941-018X

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The kinetics of interleukin-6 (IL-6)

serum concns. were analyzed in

patients with a culture verified *S. aureus* septicemia. All patients had

elevated IL-6 serum concns. on

admission. In most cases a subsequent

rapid decrease to low levels was

registered within 10 days. In most cases

changes in IL-6 serum concns. reflected

the clin. course. The raised IL-6

levels were concomitant with increases in

other inflammatory parameters

and a relation was found between IL-6

serum concns. and levels of

C-reactive protein.

L6 ANSWER 34 OF 43 MEDLINE

DUPLICATE 30

ACCESSION NUMBER: 95261963

MEDLINE

DOCUMENT NUMBER: 95261963

PubMed ID: 7743368

TITLE: Serum levels of end

products of nitric oxide synthesis

correlate positively with tumor

necrosis factor alpha and

negatively with body

temperature in patients with

postoperative abdominal

sepsis.

AUTHOR: Barthlen W; Stadler J;

Lehn N L; Miethke T; Bartels H;

Siewert J R

CORPORATE SOURCE: Department of
Surgery, Technical University, Munich,
Germany.

SOURCE: SHOCK, (1994 Dec) 2 (6)
398-401.

Journal code: 9421564. ISSN:
1073-2322.

PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
(CONTROLLED CLINICAL
TRIAL)

Journal; Article; (JOURNAL
ARTICLE)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199506
ENTRY DATE: Entered STN:
19950621

Last Updated on STN:
19950621

Entered Medline: 19950614
AB Nitric oxide (NO) has been implicated
as the principal mediator of the
catecholamine resistant vasodilation in
septic shock. In this pilot study,
we wanted to know if the serum values of
nitrite/nitrate (NO₂/NO₃), the
stable endproducts of NO biosynthesis,
are elevated in patients with
septic shock. Furthermore, we
investigated whether there is a correlation
between NO₂/NO₃ serum levels and
tumor necrosis factor
alpha or interleukin 6. NO₂/NO₃ serum
values were
significantly elevated in septic patients
compared to controls (72.1 +/-
6.1 vs. 35.7 +/- 9.2 microM, $p < .001$).
There was a significant positive
correlation between serum values of
NO₂/NO₃ and tumor necrosis factor
alpha ($r_s = 0.59$, $p < .001$). In contrast, no
correlation between NO₂/NO₃
and interleukin 6 was found. With the
exception of
body core temperature, which showed a
negative correlation with NO₂/NO₃
levels, no clinical variable turned out to
be significantly related to NO
biosynthesis. These data indicate a
potential role for NO in the clinical
course of abdominal sepsis, but points
out that more specific
data has to be evaluated by prospective
clinical studies in order to

understand the complex pathophysiologic
role of this novel mediator.

L6 ANSWER 35 OF 43 MEDLINE
DUPLICATE 31

ACCESSION NUMBER: 95025111
MEDLINE

DOCUMENT NUMBER: 95025111
PubMed ID: 7938903

TITLE: Blood cytokine and
complement levels in patients with
sepsis.

AUTHOR: Takakuwa T; Endo S;
Nakae H; Kikuchi M; Baba N; Inada K;
Yoshida M

CORPORATE SOURCE: Critical Care and
Emergency Center, Iwate Medical
University, Morioka, Japan.

SOURCE: RESEARCH
COMMUNICATIONS IN CHEMICAL
PATHOLOGY AND
PHARMACOLOGY, (1994 Jun)
84 (3) 291-300.

Journal code: 0244734. ISSN:
0034-5164.

PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article;
(JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199411
ENTRY DATE: Entered STN:
19941222

Last Updated on STN:
19941222

Entered Medline: 19941101
AB We measured serum levels of
endotoxin, cytokines, and
eicosanoids and investigated their
relationship to serum complement levels
in patients with sepsis. Serum endotoxin
(Et) levels (5.3 +/-
2.4 pg/ml) were within the normal range,
but levels of tumor necrosis
factor-alpha (TNF-alpha, 114 +/- 104.94
pg/ml), interleukin
6 (IL-6, 86.7 +/- 50.9 pg/ml), interleukin 8
(IL-8, 86.8 +/- 49.7
pg/ml), type-II phospholipase A2 (type II
PLA2, 211.3 +/- 193.9 ng/ml),
leukotriene B4 (LTB4, 88.7 +/- 27.2
pg/ml), thromboxane B2 (TXB2, 58.7 +/-
50.9 pg/ml) and 6-keto-prostaglandin F1
alpha (PGF1 alpha, 21.0 +/- 11.0
pg/ml) levels were above normal. Levels
of C3a (1088.4 +/- 83.8.7 ng/ml)

and C4a (1951.5 +/- 1697.8 ng/ml) were also above normal; C3 (66.0 +/- 25.6 mg/dl) and C4 (23.6 +/- 5.3 mg/dl) were within the normal range, and C5a was lower than the detectable limit in all but one of the subjects.

Serum TNF-alpha was significantly correlated with C3a ($p < 0.001$). Serum IL-6 had a significant negative correlation with C3 ($p = 0.002$) and C4 ($p = 0.010$). Type II PLA2 was significantly correlated with C3a ($p < 0.001$).

There were no significant correlations between serum Et or IL-8 and serum C3, C4, C3a or C4a. Our findings suggest that increased levels of TNF-alpha, IL-6, and Type II PLA2 in patients with sepsis

contribute to activation of the complement system.

L6 ANSWER 36 OF 43 MEDLINE
DUPLICATE 32

ACCESSION NUMBER: 95253988

MEDLINE

DOCUMENT NUMBER: 95253988

PubMed ID: 7735958

TITLE: Changes in skeletal muscle pO2 after administration of anti-TNF alpha-antibody in patients with severe sepsis: comparison to interleukin-

6 serum levels, APACHE II, and Elebute scores.

AUTHOR: Boekstegers P; Weidenhofer S; Zell R; Holler E; Kapsner T; Redl H; Schlag G; Kaul M; Kempeni J; Werdan K

CORPORATE SOURCE: Department of Internal Medicine I, Klinikum Grosshadern, University of Munich, Germany.

SOURCE: SHOCK, (1994 Apr) 1 (4) 246-53.

Journal code: 9421564. ISSN: 1073-2322.

PUB. COUNTRY: United States

DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL

ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199506

ENTRY DATE: Entered STN:
19950615

Last Updated on STN:

19950615

Entered Medline: 19950607

AB In 20 patients with severe sepsis, skeletal muscle pO2 was continuously measured in order to assess whether a decrease of skeletal muscle pO2 was accompanied by an improvement of sepsis after repeated administration of F(ab')2 fragments of a murine anti-TNF alpha-antibody. Abnormally high skeletal muscle pO2 decreased from 43.5 +/- 10.9 mmHg (day 0) to 36.4 +/- 10.1 mmHg within 24 h after the first administration of anti-TNF alpha-antibody (day 1, $p = .006$, $n = 20$) and remained at 34.6 +/- 7.7 mmHg thereafter (mean day 2-7, $p = .004$). The decrease of skeletal muscle pO2 within 24 h exceeded 5 mmHg (-7 to -19 mmHg) in 11 patients in contrast to nine patients (-4 to +4 mmHg). Only in the patients showing a decrease of skeletal muscle pO2 did sepsis improve as determined by Elebute score, APACHE II score, and interleukin-6 serum levels. The change of skeletal muscle pO2 within 24 h was associated with a change of interleukin-6 serum levels within 24 h ($r = .5$, $n = 20$), with a change of Elebute score ($r = .7$, $n = 20$) and of APACHE II score ($r = .62$). These data suggest that a decrease of skeletal muscle pO2 might be an early indicator of improvement of sepsis after administration of anti-TNF alpha-antibodies.

L6 ANSWER 37 OF 43 MEDLINE
DUPLICATE 33

ACCESSION NUMBER: 93056706

MEDLINE

DOCUMENT NUMBER: 93056706

PubMed ID: 1431255

TITLE: Effectiveness of a human monoclonal anti-endotoxin antibody (HA-1A) in gram-negative sepsis: relationship to endotoxin and cytokine levels.

COMMENT: Comment in: J Infect Dis. 1993 Jul;168(1):246-8

AUTHOR: Wortel C H; von der Mohlen M A; van Deventer S J; Sprung C

L; Jastremski M; Lubbers M J;
Smith C R; Allen I E; ten
Cate J W

CORPORATE SOURCE: Department of
Gastroenterology, University of Amsterdam,
Netherlands.

SOURCE: JOURNAL OF
INFECTIOUS DISEASES, (1992 Dec) 166
(6) 1367-74.

Journal code: 0413675. ISSN:
0022-1899.

PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)

Journal; Article; (JOURNAL
ARTICLE)
(MULTICENTER STUDY)
(RANDOMIZED CONTROLLED

TRIAL)

LANGUAGE: English
FILE SEGMENT: Abridged Index

Medicus Journals; Priority Journals

ENTRY MONTH: 199212

ENTRY DATE: Entered STN:
19930122

Last Updated on STN:
19930122

Entered Medline: 19921222

AB Gram-negative sepsis is caused by
endotoxin-induced release of

tumor necrosis factor (TNF) and other
cytokines. HA-1A is a human

monoclonal antibody that binds
specifically to endotoxin. HA-1A should

prevent death in endotoxemic patients
and reduce serum

levels of TNF and interleukin-6 (IL-6).
This

hypothesis was tested in 82 septic
patients who were randomly allocated to

receive a single intravenous 100-mg
dose of HA-1A or placebo. Pretreatment

endotoxemia was detected in 27 patients
(33%). Death occurred within 28

days of treatment in 8 (73%) of 11
placebo recipients and in 5 (31%) of 16

HA-1A recipients ($P = .02$). The median
decrease in serum TNF level 24 h

after treatment was 12 ng/L in patients
given HA-1A and 0 ng/L in placebo

recipients ($n = 65$; $P = .04$). For IL-6, this
was 204 ng/L in patients

given HA-1A and 44 ng/L in placebo
recipients ($n = 67$; $P = .4$). Thus,

HA-1A reduces mortality in septic
patients with endotoxemia and lowers
serum TNF levels.

L6 ANSWER 38 OF 43 MEDLINE
DUPLICATE 34

ACCESSION NUMBER: 93101937

MEDLINE

DOCUMENT NUMBER: 93101937

PubMed ID: 1465578

TITLE: Kinetics of serum levels of
interleukin-6 in *Staphylococcus*
aureus

septicemia.

AUTHOR: Soderquist B; Sundqvist K
G; Vikerfors T

CORPORATE SOURCE: Department of
Infectious Diseases, Orebro Medical Center
Hospital, Sweden.

SOURCE: SCANDINAVIAN
JOURNAL OF INFECTIOUS DISEASES,
(1992) 24 (5)

607-12.

Journal code: 0215333. ISSN:
0036-5548.

PUB. COUNTRY: Sweden

DOCUMENT TYPE: Journal; Article;
(JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199301

ENTRY DATE: Entered STN:
19930205

Last Updated on STN:
19970203

Entered Medline: 19930121

AB The kinetics of IL-6 serum
concentrations were analyzed in 17 patients

with a culture verified *Staphylococcus*
aureus septicemia. The analyses

were performed using an antigen capture
immunoassay. All patients had

elevated IL-6 serum concentrations on
admission. In most cases a

subsequent rapid decrease to low levels
was registered within 10 days. The

IL-6 serum concentrations reflected the
clinical course. In sera sampled

on admission a relationship was found
between IL-6 serum concentrations
and levels of C-reactive protein.

L6 ANSWER 39 OF 43 MEDLINE
DUPLICATE 35

ACCESSION NUMBER: 92306319

MEDLINE

DOCUMENT NUMBER: 92306319

PubMed ID: 1611704

TITLE: Polymicrobial sepsis
selectively activates peritoneal but
not alveolar macrophages to
release inflammatory mediators
(interleukins-1 and -6 and tumor
necrosis factor).

AUTHOR: Ayala A; Perrin M M;
Kisala J M; Ertel W; Chaudry I H
CORPORATE SOURCE: Department of
Surgery, Michigan State University, East
Lansing 48824.

CONTRACT NUMBER: R01 GM 37127
(NIGMS)

SOURCE: CIRCULATORY SHOCK,
(1992 Mar) 36 (3) 191-9.

Journal code: 0414112. ISSN:
0092-6213.

PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article;
(JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199207
ENTRY DATE: Entered STN:
19920807

Last Updated on STN:
19920807

Entered Medline: 19920727

AB While a number of clinical studies
indicate that elevated serum cytokine
[interleukin-1 (IL-1), interleukin-6 (IL-6),
and tumor

necrosis factor (TNF)] levels are
associated with enhanced mortality in
sepsis, the time course and the role that
different macrophage (M

phi) populations play in releasing these
cytokines remain to be
determined. To study this, polymicrobial
sepsis was induced in

C3H/HeN mice by cecal ligation and
puncture (CLP). The animals were then
sacrificed at 1, 4, or 24 hr post-CLP.
Blood was taken for serum cytokine
level determination. Macrophages, of
either peritoneal (PM phi) or

alveolar (AM phi) origin, were harvested
by lavage, and their innate vs.

inducible cytokine productive capacities
were assessed by incubation with
or without endotoxin (lipopolysaccharide;
LPS). Serum

levels of TNF were significantly
enhanced 1 hr post-CLP (CLP = 3.8
+/- 2.4* vs. sham = 0.4 +/- 0.9 U/ml; P
less than 0.05 by t test).

However, not until 4 hr post-CLP were
marked increases in IL-6 observed
(CLP = 318.0 +/- 209.0* vs. sham = 1.1
+/- 0.5 U/ml), which remained
elevated through 24 hr post-CLP (CLP =
11.3 +/- 15.0* vs. sham = 0.03 +/-
0.02 U/ml). Cytokine release (IL-1, IL-6,
TNF) from PM phi (without the
addition of LPS) was detectable only in
cells harvested 1 h following CLP.

Alveolar M phi from septic mice showed
little in vivo activation. Septic

PM phi IL-1 and IL-6 production was
markedly depressed at all time points
with LPS stimulation, but TNF release
remained unaltered.(ABSTRACT
TRUNCATED AT 250 WORDS)

L6 ANSWER 40 OF 43 MEDLINE
DUPLICATE 36

ACCESSION NUMBER: 93047045
MEDLINE

DOCUMENT NUMBER: 93047045
PubMed ID: 1423922

TITLE: Production of tumor necrosis
factor-alpha and interleukin-6
in mice infected with group B

streptococci.

AUTHOR: Teti G; Mancuso G;
Tomasello F; Chiofalo M S
CORPORATE SOURCE: Istituto di
Microbiologia, Facolta di Medicina,
Universita

di Messina, Italy.

SOURCE: CIRCULATORY SHOCK,
(1992 Oct) 38 (2) 138-44.

Journal code: 0414112. ISSN:
0092-6213.

PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article;
(JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199212
ENTRY DATE: Entered STN:
19930122

Last Updated on STN:
19930122

Entered Medline: 19921211

AB Group B streptococci (GBS) are a
leading cause of sepsis and
meningitis in neonates. Since cytokines
are thought to play an important
role in septic shock, we have studied
serum levels of

tumor necrosis factor-alpha (TNF alpha) and interleukin-6 (IL-6) in BALB/c mice infected with type III GBS. TNF alpha and

IL-6 were detected by the L929 cytotoxicity and the B9 proliferation assays, respectively, in serial serum samples obtained after infection.

After i.p. challenge with an LD50, serum TNF alpha rose above baseline values as early as 3 hr, peaked at 7 hr, and returned to baseline values at 20 hr. IL-6 serum levels rose concomitantly with

TNF alpha, peaking 8 hr after challenge. No serum TNF alpha activity was detected in the course of sublethal infections. However, a transient rise

in TNF alpha levels was observed after i.v. inoculation of high numbers (greater than or equal to 1×10^8) of heat-killed GBS. When groups of mice were injected i.v. with a single dose of anti-TNF alpha rabbit serum

2 hr before challenge with an LD90 or LD30, no effect was noted in terms of survival, although the serum TNF alpha peak was completely abrogated.

Serum TNF alpha does not seem to play an obligatory role in GBS-induced lethality of adult mice. However, further studies are needed to assess better the role of this cytokine in the pathogenesis of GBS sepsis

L6 ANSWER 41 OF 43 MEDLINE
DUPLICATE 37

ACCESSION NUMBER: 92351276
MEDLINE

DOCUMENT NUMBER: 92351276
PubMed ID: 1641756

TITLE: Spin trap salvage from
endotoxemia: the role of cytokine
down-regulation.

AUTHOR: Pogrebniak H W; Merino
M J; Hahn S M; Mitchell J B; Pass H
I

CORPORATE SOURCE: Thoracic
Oncology Section, National Cancer Institute,
National Institutes of Health,
Bethesda, MD 20892.

SOURCE: SURGERY, (1992 Aug)
112 (2) 130-9; discussion 138-9.

Journal code: 0417347. ISSN:
0039-6060.

PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article;
(JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: Abridged Index

Medicus Journals; Priority Journals

ENTRY MONTH: 199208

ENTRY DATE: Entered STN:
19920911

Last Updated on STN:
19920911

Entered Medline: 19920828
AB BACKGROUND. The spin trap alpha-phenyl-N-tert-butyl-nitron (PBN) affords protection from the lethality of septic (lipopolysaccharide) shock. We hypothesized that PBN may work through down-regulation of the sepsis-induced cytokine cascade.

METHODS. C3H/HEN mice received 30 mg/kg lipopolysaccharide 15 minutes after pretreatment with PBN or vehicle. Animals were monitored for differences in behavior,

histopathologic studies, survival, and serum levels of tumor necrosis factor (TNF-alpha),

interferon-gamma (IFN-gamma), and interleukin-6 (IL-6) after

lipopolysaccharide. Northern blot analyses of TNF, IFN-gamma, c-fos, and IL-6 transcripts were also performed.

RESULTS. Seventy-two-hour survival was significantly higher in the PBN-treated (59/60) compared with the saline-treated animals (13/60; $p < 0.005$), and the PBN group exhibited a blunted endotoxemic

response. TNF levels were significantly lower in the PBN-treated animals at 1 to 6 hours, whereas IFN-gamma levels were depressed at 8 hours. PBN

down-regulated TNF transcription at 30 minutes, with maximum lowering of all cytokine transcripts at 6 hours. PBN depressed c-fos transcription within 15 minutes of lipopolysaccharide injection.

CONCLUSIONS. Spin trap protection from endotoxemia may be related to interruption of the cytokine network, with profound effects on transcription and protein elaboration.

Such compounds may prove useful in not only sepsis but also other cytokine-free radical-related pathophysiologic alterations.

L6 ANSWER 42 OF 43 MEDLINE
DUPLICATE 38

ACCESSION NUMBER: 91127631

MEDLINE

DOCUMENT NUMBER: 91127631

PubMed ID: 1992764

TITLE: In vivo biologic and
immunohistochemical analysis of
interleukin-1 alpha, beta and
tumor necrosis factor during
experimental endotoxemia.
Kinetics, Kupffer cell
expression, and glucocorticoid
effects.

AUTHOR: Chensue S W; Terebuh P
D; Remick D G; Scales W E; Kunkel S

L

CORPORATE SOURCE: Department of
Pathology, Veterans Affairs Medical Center,
Ann Arbor, MI 48105.

CONTRACT NUMBER: HL31237 (NHLBI)

HL31963 (NHLBI)

HL35276 (NHLBI)

SOURCE: AMERICAN JOURNAL
OF PATHOLOGY, (1991 Feb) 138 (2) 395-
402.

Journal code: 0370502. ISSN:
0002-9440.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article;
(JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Abridged Index

Medicus Journals; Priority Journals

ENTRY MONTH: 199103

ENTRY DATE: Entered STN:
19910405

Last Updated on STN:
19970203

Entered Medline: 19910314

AB Using a model of sepsis induced by
parenteral challenge of mice
with bacterial lipopolysaccharide (LPS),
the authors analyzed the in vivo
expression of interleukin-1 (IL-1)
alpha, beta and tumor necrosis factor
(TNF). Both TNF and IL-1 alpha, beta
were detected in hepatic sinusoidal
macrophages (Kupffer cells),
immunohistochemically. Kinetic analysis
showed a clear sequence of synthesis.
Tumor necrosis factor was produced
first, reaching maximal expression at 1
hour after LPS challenge, then

rapidly disappeared. IL-1 beta followed,
reaching maximal expression at 2
to 3 hours, then dropped off by 6 hours.
Interleukin-1 alpha expression
reached a peak at 6 hours and had
disappeared by 18 hours. Analysis of
serum bioactivity also revealed
sequential expression that correlated with
immunohistochemical findings. Tumor
necrosis factor was maximal at 1 hour
and IL-1 at 6 hours. The IL-1 bioactivity
was not due to
interleukin-6 (IL-6), as this was depleted
from
specimens by immunoabsorption. Also
IL-6 bioactivity reached maximal
levels at 3 hours, earlier than IL-1.
Pretreatment with 4 mg/kg
dexamethasone significantly decreased
Kupffer cell expression of TNF and
IL-1 alpha (about 80% and 60%
suppression, respectively) but had less
effect on IL-1 beta expression (about
30% suppression). Accordingly,
serum levels of TNF were suppressed by
75% while serum
IL-1 was decreased by 39%, indicating
differential sensitivity of these
cytokines to glucocorticoids. Endogenous
corticosteroid levels increased
as TNF levels decreased, supporting the
contention that glucocorticoids
regulate TNF synthesis. In contrast, IL-1
levels rose concurrently with
corticosterone. These data indicate a
sequential activation of cytokine
gene expression in vivo, which may be
critical to the cascade of events
leading to septic shock, and provide
evidence that Kupffer cells are a
major source of cytokines in
endotoxemia. Finally, the differential
sensitivity of cytokine expression to
glucocorticoids may in part explain
the inadequacy of the latter in the
treatment of sepsis.

L6 ANSWER 43 OF 43 MEDLINE
DUPLICATE 39

ACCESSION NUMBER: 90228909

MEDLINE

DOCUMENT NUMBER: 90228909

PubMed ID: 2184115

TITLE: Excessive in vitro bacterial
lipopolysaccharide-induced

production of monokines in
cirrhosis.
AUTHOR: Deviere J; Content J;
Denys C; Vandenbussche P; Schandene
L; Wybran J; Dupont E
CORPORATE SOURCE: Department of
Gastroenterology, Hopital Erasme, Brussels
Free University, Belgium.
SOURCE: HEPATOLOGY, (1990
Apr) 11 (4) 628-34.

Journal code: 8302946. ISSN:
0270-9139.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article;
(JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199005
ENTRY DATE: Entered STN:
19900706

Last Updated on STN:
19900706

Entered Medline: 19900525

AB The objective of this study was to
analyze monokine production by
peripheral blood mononuclear cells from
patients with alcoholic cirrhosis.

The capacity of peripheral blood
mononuclear cells and purified monocytes
from these patients to produce tumor
necrosis factor alpha, interleukin 1
beta, and interleukin 6 was investigated.
Spontaneous
production of tumor necrosis factor alpha,
interleukin 6

and interleukin 1 beta was similar in
cirrhotic and healthy subjects, but
serum levels of interleukin 6 (less
than 2 U/ml vs. 9.5 +/- 3 U/ml) and tumor
necrosis factor alpha (3.1 +/-
1.2 pg/ml vs. 12.0 +/- 1.2 pg/ml) were
significantly higher in cirrhotic
patients. However, peripheral blood
mononuclear cells or purified
monocytes from patients with alcoholic
liver cirrhosis, stimulated in
vitro with Escherichia coli
lipopolysaccharide, displayed a marked
increase of tumor necrosis factor alpha,
interleukin 1 beta and
interleukin 6 secretions compared with
healthy controls.

A striking feature of this overproduction
was its reversibility as
assessed by allowing cells to rest in vitro
without lipopolysaccharide for

1 to 7 days before stimulation. In such
conditions, tumor necrosis factor
alpha and interleukin 6 secretions
declined to levels
present in healthy subjects in whom
production remained stable, whereas
interleukin 1 beta secretion markedly
decreased in both groups to the
point where no difference could be seen.
This reversible oversecretion of
cytokines after lipopolysaccharide
stimulation, along with the lack of
abnormality of spontaneous cytokine
secretion, suggests that monocytes in
these patients may have undergone an in
vivo activation process analogous
to a priming phenomenon. The in vitro
activation with lipopolysaccharide
may represent the correlate of in vivo
endotoxemia observed during acute
events such as sepsis.(ABSTRACT
TRUNCATED AT 250 WORDS)

=> s tnf (W) antibodies or tumor (W)
necrosis (w) factor (w) antibodies

4 FILES SEARCHED...

L7 891 TNF (W) ANTIBODIES OR
TUMOR (W) NECROSIS (W) FACTOR (W)
ANTIBODI
ES

=> s l6 and l7

L8 1 L6 AND L7

=> d l8 1- ibib,abs

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ANSWERS - CONTINUE? Y/(N):y

L8 ANSWER 1 OF 1 CAPLUS

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ACCESSION NUMBER: 1995:842658

CAPLUS

DOCUMENT NUMBER: 123:225947

TITLE: Use of anti-TNF
antibodies as

drugs in treating diseases
involving elevated

interleukin-6 serum levels
INVENTOR(S): Stenzel, Roswitha;

Kaul, Martin; Daum, Lothar;

Kempeni, Joachim; Raab,
Christa; Schaefer, Sibylle

PATENT ASSIGNEE(S): Knoll A.-G.,
Germany

SOURCE: PCT Int. Appl., 18 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO. KIND DATE
APPLICATION NO. DATE

WO 9520978 A1 19950810 WO
1995-EP291 19950127
W: AU, BR, BY, CA, CN, CZ, FI, HU,
JP, KR, KZ, MX, NO, NZ, PL, RU,
SI, UA, US
RW: AT, BE, CH, DE, DK, ES, FR,
GB, GR, IE, IT, LU, MC, NL, PT, SE
DE 4409513 C1 19951019 DE
1994-4409513 19940319
IL 112427 A1 19981206 IL
1995-112427 19950124
CA 2182723 AA 19950810 CA
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AU 9515201 A1 19950821 AU
1995-15201 19950127
CN 1140414 A 19970115 CN
1995-191517 19950127
JP 09509411 T2 19970922 JP
1995-520363 19950127
BR 9506741 A 19971021 BR
1995-6741 19950127
EP 804236 A1 19971105 EP
1995-906353 19950127
R: AT, BE, CH, DE, DK, ES, FR, GB,
GR, IT, LI, LU, NL, SE, PT, IE, SI
HU 76875 A2 19971229 HU
1996-2169 19950127
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1995-84100744 19950127
CZ 290843 B6 20021016 CZ
1996-2322 19950127
ZA 9500956 A 19951011 ZA
1995-956 19950207
FI 9603101 A 19960806 FI
1996-3101 19960806

NO 9603280 A 19961004 NO
1996-3280 19960806
MX 9603243 A 20000228 MX
1996-3243 19960807
US 6235281 B1 20010522 US
1996-687328 19960807
AU 9915495 A1 19990401 AU
1999-15495 19990208
US 2001010819 A1 20010802
US 2001-782290 20010214
PRIORITY APPLN. INFO.: DE
1994-4403669 A 19940207
DE 1994-4409513
A 19940319
AU 1995-15201
A3 19950127
WO 1995-EP291
W 19950127
US 1996-687328
A1 19960807
AB Tumor necrosis factor (TNF)
antagonists, esp. anti-TNF
antibodies and their fragments, are useful
in prodn. of drugs to
treat diseases characterized by elevated
interleukin-6
serum levels, e.g. sepsis.

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FULL ESTIMATED COST
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DISCOUNT AMOUNTS (FOR QUALIFYING
ACCOUNTS) SINCE FILE TOTAL
ENTRY

SESSION
CA SUBSCRIBER PRICE
-3.91 -3.91

STN INTERNATIONAL LOGOFF AT
18:14:53 ON 19 MAR 2003

TITLE: Significance of systemic inflammatory response syndrome at cardiopulmonary bypass.
AUTHOR: Furunaga A; Tsuboi H; Itoh H; Kawamura T; Minami Y; Gohra H; Katoh T; Fujimura Y; Esato K
CORPORATE SOURCE: First Department of Surgery, Yamaguchi University School of Medicine, Ube, Japan.

SOURCE: NIPPON KYOBU GEKA GAKKAI ZASSHI. JOURNAL OF THE JAPANESE

ASSOCIATION FOR THORACIC SURGERY, (1996 Jun) 44 (6) 790-4.

Journal code: 19130180R.

ISSN: 0369-4739.

PUB. COUNTRY: Japan

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: Japanese

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199609

ENTRY DATE: Entered STN: 19960924

Last Updated on STN:

19960924

Entered Medline: 19960917

AB Systemic Inflammatory Response Syndrome (SIRS) is a new concept of entry criteria for sepsis. This concept, when applied to area of

Multiple Organ Failure (MOF), is considered to be a preparatory state for MOF. To study the significance of SIRS state at cardiac surgery, we

measured the body temperature, white blood cell count, respiratory rate and heart rate of 18 patients who

underwent elective cardiac surgery, from the 1st post-operative day to the 7th post-operative day. We also measured

Interleukin-6 and 8 (IL-6 and IL-8) to understand the

relationship between the SIRS state and inflammatory cytokines just after

cardiopulmonary bypass (CPB), at the 1st, 3rd and 6th postoperative day.

The result was as follows: Patients with CPB more than 120 minutes have more frequency and longer duration of SIRS than patients with CPB less than 120 minutes. Serum levels of IL-8 at SIRS state

were revealed statistically higher than at non-SIRS case. Duration of SIRS

state was related to CPB time and serum levels of IL-6

and IL-8 just after CPB. We concluded that SIRS state is an indication for anti-cytokine therapy to prevent MOF, and it is important to shorten CPB time in order to decrease the duration of SIRS.

L6 ANSWER 27 OF 43 MEDLINE
DUPLICATE 24

ACCESSION NUMBER: 97048569

MEDLINE

DOCUMENT NUMBER: 97048569

PubMed ID: 8893405

TITLE: Dynamics of blood cytokine concentrations in patients with bacteremic infections.

AUTHOR: Kragsbjerg P; Holmberg H; Vikersborg T

CORPORATE SOURCE: Department of Infectious Diseases, Orebro Medical Center Hospital, Sweden.

SOURCE: SCANDINAVIAN JOURNAL OF INFECTIOUS DISEASES, (1996) 28 (4)

391-8.

Journal code: 0215333. ISSN:

0036-5548.

PUB. COUNTRY: Sweden

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199701

ENTRY DATE: Entered STN: 19970219

Last Updated on STN:

19970219

Entered Medline: 19970128

AB Cytokines play a major role in the pathophysiology of sepsis and

septic shock. Using enzyme immunoassays the acute serum

levels of interleukin-6 (IL-6), tumor necrosis

factor-alpha (TNF-alpha), granulocyte-colony stimulating factor (G-CSF),

interleukin-8 (IL-8), and leukemia inhibitory factor (LIF) were

investigated in 90 patients with positive blood cultures and clinical

signs of infection. In 27 patients samples were obtained on admission,

after 1, 4, 12, 18, and 24 h, and then daily. The acute serum

RC110.528

levels of IL-6, TNF-alpha, G-CSF, and IL-8 were significantly

higher among patients with severe sepsis. Patients with

Gram-negative infection had significantly higher levels of TNF-alpha on admission than did patients with Gram-positive infections ($p = 0.0008$).

The levels of IL-6, G-CSF and, to some extent, TNF-alpha decreased rapidly in survivors within the first 24 h of admission to hospital and institution of treatment. LIF was detected in 8/90 in both survivors and nonsurvivors.

L6 ANSWER 28 OF 43 EMBASE

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B.V.DUPLICATE 25

ACCESSION NUMBER: 97046690

EMBASE

DOCUMENT NUMBER: 1997046690

TITLE: [The role of cytokines in the diagnosis of sepsis].

STELLENWERT VON
ZYTOKINEN IN DER SEPSIS-
DIAGNOSTIK.

AUTHOR: Fraunberger P.; Walli
A.K.; Seidel D.

CORPORATE SOURCE: Dr. P.
Fraunberger, Institut für Klinische Chemie,
Klinikum

Grosshadern, Universität
München, Marchioninistrasse 15,
D-81366 München, Germany

SOURCE: Infusionstherapie und
Transfusionsmedizin, (1996) 23/SUPPL.
4 (109-116).

Refs: 77

ISSN: 1019-8466 CODEN:

IRANEE

COUNTRY: Switzerland

DOCUMENT TYPE: Journal; Conference
Article

FILE SEGMENT: 006 Internal
Medicine

026 Immunology, Serology
and Transplantation

029 Clinical Biochemistry

LANGUAGE: German

SUMMARY LANGUAGE: German; English

AB Both clinical and experimental studies
show that cytokines play a central
role in sepsis. Inflammatory conditions
lead to release of

cytokines which coordinate various
components of the immune system. Even
though several cytokines are involved in
the complex process of the
development of sepsis, only interleukin 1
(IL-1),

interleukin 6 (IL-6), tumor necrosis factor
alpha (TNF),

interleukin 8 (IL-8) and interleukin 10 (IL-
10) can be measured accurately

with the facilities available in clinical
laboratories. Certain cytokine

antagonists such as soluble TNF
receptors and interleukin 1 receptor

antagonist are also found in measurable
amounts in serum. Serum

levels of IL-6 appear to correlate with the
organ dysfunction and

have high prognostic value. Even though
TNF plays a central role in

sepsis, the serum levels show
considerable

variation owing to its short biological half
life and therefore render

this parameter less suitable for the
follow-up of sepsis. Recent

studies show the usefulness of the
measurement of TNF receptors in

sepsis. These receptors have a longer
biological half life than

TNF and can be measured within a few
hours by automated methods in a
routine clinical chemistry laboratory.

L6 ANSWER 29 OF 43 CAPLUS

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ACCESSION NUMBER: 1995:842658

CAPLUS

DOCUMENT NUMBER: 123:225947

TITLE: Use of anti-TNF
antibodies as drugs in treating
diseases involving elevated
interleukin-6 serum levels

INVENTOR(S): Stenzel, Roswitha;
Kaul, Martin; Daum, Lothar;

Kempner, Joachim; Raab,
Christa; Schaefer, Sibylle

PATENT ASSIGNEE(S): Knoll A.-G.,
Germany

SOURCE: PCT Int. Appl., 18 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION: